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LESIONS OF THE SUPRASPINATUS TENDON

DEGENERATION, RUPTURE AND CALCIFICATION

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The purpose of this paper is to make a survey of the literature on lesions of the tendons of the short rotator muscles of the shoulder, namely, the supraspinatus, infraspinatus, teres minor and subscapularis. As has been pointed out by Codman,[1] lesions of the shoulder tendons, notably rupture of the supraspinatus tendon, are significant because of the long duration of the disability produced when they are not recognized early. This is particularly important in the laboring classes, for the disability produced by rupture of the supraspinatus tendon may be sufficient to prevent a laborer from working for two years.[2]

I. ANATOMIC CONSIDERATIONS

Gross Anatomy.—The anatomy of the shoulder joint will be considered briefly in order to give a clear concept of the subacromial bursa, the tendons of the short rotator muscles of the shoulder, namely the supraspinatus, infraspinatus, teres minor and subscapularis, and the tendon of the long head of the biceps muscle. If the anatomy and function of these structures are clearly pictured, the understanding of the conditions affecting them is greatly enhanced.

The subacromial bursa is a synovial bursa occurring beneath the deltoid muscle, the coracoacromial ligament and the acromion and intervening between these structures and the supraspinatus tendon.[3] The bursa is roughly circular in outline, fitting equally over the ligaments and their insertions into the head of the humerus, like a skull cap. Codman [1h] remarked that "the first time one cuts into a normal bursa one is startled to find how much the base looks like the shoulder joint itself. One cannot distinguish by sight the line between the portions which are on bone, or on tendon beneath the shiny base." The bursa increases in size with age, being

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1. Codman, E. A.: (*a*) Some Points on the Diagnosis and Treatment of Certain Neglected Minor Surgical Lesions, Boston M. & S. J. **150**:371, 1904; (*b*) Stiff and Painful Shoulders: The Anatomy of the Subdeltoid or Subacromial Bursa and Its Clinical Importance; Subdeltoid Bursitis, ibid. **154**:613, 1906; (*c*) Bursitis Subacromalis or Periarthritis of the Shoulder Joint: (Subdeltoid Bursitis), ibid. **159**:533, 576, 615, 677 and 723, 1908; (*d*) Complete Rupture of the Supraspinatus Tendon: Operative Treatment with Report of Two Successful Cases, ibid. **164**:708, 1911; (*e*) On Stiff and Painful Shoulders, as Explained by Subacromial Bursitis and Partial Rupture of the Tendon of the Supraspinatus, ibid. **165**:115, 1911; (*f*) Obscure Lesions of the Shoulder: Rupture of the Supraspinatus Tendon, ibid. **196**:381, 1927; (*g*) Rupture of the Supraspinatus Tendon, Surg., Gynec. & Obst. **52**:579, 1931; (*h*) The Shoulder: Rupture of the Supraspinatus Tendon and Other Lesions in or About the Subacromial Bursa, Boston, The Author, 1934; (*i*) Rupture of Supraspinatus, Am. J. Surg. **42**: 603, 1938.

2. Codman.[1b,i]

3. (*a*) Gray, H.: Anatomy, Descriptive and Applied, edited by T. B. Johnston, ed. 26, New York, Longmans, Green & Co., 1935. (*b*) Piersol, G. A.: Human Anatomy, Philadelphia, J. B. Lippincott Company, 1907, vol. 2. (*c*) Codman.[1b,h]

1.5 cm. in diameter in a newly born infant and 3 to 7 cm.[4] in diameter in a fully developed adult. Its function is to permit the upper end of the humerus with its capsule to glide easily under the coracoacromial ligament and the acromion during abduction.[5] The bursa has been considered to be indispensable in abduction and rotation of the humerus,[5b] but Moseley[6] has removed the bursa in 2 cases and had perfect function of the arm.

The origins of the four short rotator muscles can be reviewed in any textbook of anatomy. The important point is that their tendons flatten out and blend almost indistinguishably with the floor of the subacromial bursa and capsule of the shoulder joint.[7] The edges of the tendons of the four muscles approximate each other, and it is often difficult to tell where one stops and the next begins.[8] This fused structure Codman[1h] called "the musculo-tendinous cuff." The average length of the supraspinatus tendon on both the right and the left side is 2.25 cm.[7b]

The attachment of the tendons of the short rotator muscles takes place through most of the upper half of the sulcus, which is called the anatomic neck of the humerus. The heavier portions of the tendons are inserted on the facets situated on the greater tuberosity. Skinner[9] claimed that the muscular portion decreases with age and is replaced by fibrous tissue. This aponeurosis then fuses with the capsule of the shoulder joint. This view, however, is refuted by the work of Lindblom,[10] who found that the length of the tendon compared with the width of the head of the humerus was 9:14 = 0.64 (8 cases) in fetuses and children, and 73:131 = 0.56 (27 cases) in adults. Other measurements[7b] of tendons showed no increase in length once adult life had been reached.

Function.—The functions of the short rotator muscles of the arm, especially the supraspinatus, have been the subject of a great deal of controversy. Each author has to a certain extent been correct in his interpretation, and it is possible to combine their various views to give a complete picture. It must be realized at the outset that the function of any muscle depends not only on the direction of its force but on its training. The anatomy of the insertion of the short rotator cuff is such that all the muscles composing it must work together. Stevens[11] stated that the subscapularis muscle on one side and the infraspinatus and teres minor muscles on the other act as a sling around the anatomic neck of the humerus, keeping the head of the humerus against the glenoid cavity during abduction. Since their line of pull passes through the fulcrum of the lever, their action does not hinder abduction.

The supraspinatus tendon acts as an abductor of the arm.[12] Codman found that when the deltoid is paralyzed by a lesion of the circumflex nerve the patient

4. (*a*) Wilson, P. D.: Complete Rupture of the Supraspinatus Tendon, J. A. M. A. **96**:433 (Feb. 7) 1931. (*b*) Codman.[1h]

5. Codman.[1b, h] Wilson.[4a]

6. Moseley, H. F.: Personal communication to the author.

7. (*a*) McKeown, E. G.: Shoulder Joint Injury: Rupture of the Supraspinatus Tendon, Journal-Lancet **55**:38, 1935. (*b*) Wilson, C. L.; and Duff, G. L.: A Pathological Study of Degeneration and Rupture of the Supraspinatus Tendon, to be published. (*c*) Codman.[1h] Wilson.[4a]

8. Laird, R. C.: Complete Rupture of the Supraspinatus Tendon, Bull. Acad. Med., Toronto **14**:111, 1941. Footnote 7*c*.

9. Skinner, H. A.: Anatomical Considerations Relative to Rupture of the Supraspinatus Tendon, J. Bone & Joint Surg. **19**:137, 1937.

10. Lindblom, K.: On Pathogenesis of Ruptures of the Tendon Aponeurosis of the Shoulder Joint, Acta radiol. **20**:563, 1939.

11. Stevens, J. H.: Action of the Short Rotators of the Arm, Am. J. M. Sc. **138**:870, 1909.

12. (*a*) Duchenne, G. B. A.: Physiologie des mouvements démontreé à l'aide de l'expérimentation électrique et de l'observation clinique, Paris, J. B. Baillière & fils, 1867. (*b*) Johnston,

(Footnote continued on next page)

can still feebly abduct the arm. If he cannot, then operation will reveal a complete rupture of the supraspinatus.[1h] Smith and Christensen [13] are the only authors who have not concurred with this statement. Moseley,[14] by injecting procaine hydrochloride into a ruptured supraspinatus tendon and thus removing pain, has shown that abduction is still possible but much weakened. The loss of abduction in a case of rupture of the supraspinatus tendon is therefore due to pain. Numerous authors [15] have contended that the supraspinatus muscle prevents the head of the humerus from slipping up out of the glenoid cavity, but Stevens [11] claimed that, acting alone, the upward and inward pull of the supraspinatus and deltoid muscles would actually pull the greater tuberosity against the under surface of the acromial arch. Codman [1h] advanced the idea of "scapulo-humeral rhythm." By this he meant that as the humerus and scapula move in abduction the direction of the lines of muscle pull changes, so that the supraspinatus muscle has the function both of an abductor and of a stabilizer but in different phases of abduction. It acts as an abductor up to the horizontal position, and from there it acts only as a stabilizer of the shoulder joint.

Martin [16] has pointed out that as the humerus is raised in the coronal plane to the upright position it rotates laterally through 180 degrees, while when it is raised in the sagittal plane no rotation occurs. He showed that if the supraspinatus and deltoid muscles raise the arm in the coronal plane, they also act as lateral rotators. It should be noted that abduction of the humerus occurs in the plane of the body of the scapula [17] (not the plane of the trunk) and carries the arm forward and laterally away from the trunk.

The tendon of the long head of the biceps muscle [3a] ascends the bicipital groove, becomes encased in the synovial membrane of the shoulder joint, and enters the joint through an opening in the capsular ligament. It then passes over the head of the humerus and is inserted into the supraglenoid tubercle at the apex of the glenoid cavity. It is held in the bicipital groove by the transverse humeral ligament and a fibrous expansion from the pectoralis major muscle. Thus, the biceps muscle acts as a stabilizer of the humeroglenoid joint in abduction.[18]

Microscopic Anatomy of the Supraspinatus Tendon and Its Insertion into the Humerus.—The muscle cells run into the tendinous portion and end rather abruptly. The tendinous portion consists of primary bundles of collagenous fibers with their rows of fibroblasts grouped into secondary bundles by septums of loose fibrillar connective tissue. The base of the subacromial bursa and the capsule of the shoulder joint lie on either side of the tendon and form a considerable part of the total depth of the structure of the tendon.[7b] The vascular supply of tendons runs mostly in the loose septal connective tissue. Normal tendons are poor in blood vessels, particularly in adult life. During youth they are more richly

T. B.: Movements of the Shoulder Joint: Plea for Use of "Plane of Scapula" as Plane of Reference for Movements Occurring at Humero-Scapular Joints, Brit. J. Surg. **25**:252, 1937. (*c*) Codman.[1g,h,i] (*d*) Skinner.[9] (*e*) Stevens.[11]

13. Smith, J. F., and Christensen, H. H.: Deltoid Paralysis Following Shoulder Injuries, Surg., Gynec. & Obst. **41**:451, 1925.

14. Moseley, H. F.: Rupture of the Supraspinatus Tendon, Canad. M. A. J. **41**:280, 1939.

15. (*a*) Gray, C. H.: Rupture of Supraspinatus Tendon, Lancet **1**:483, 1938. (*b*) Moseley.[14] (*c*) Wilson.[4a]

16. Martin, C. P.: Movements of the Shoulder Joint with Special Reference to Rupture of the Supraspinatus Tendon, Am. J. Anat. **66**:213, 1940.

17. Gray.[3a] Johnston.[12b]

18. (*a*) Moseley, H. F.: Shoulder Pain, Canad. M. A. J. **46**:361, 1942. (*b*) Codman.[1h] (*c*) Moseley.[14] (*d*) Moseley.[6] Skinner.[9]

vascularized.[19] There are slits seen between the primary collagenous bundles, with a fibroblast seen usually on one side, never on both sides. Sobotta [19c] suggested that these slits contain a cement substance fastening the tendon bundles together. They may serve some such function or may be simply artefacts. There seems to be no reason to assume, as Howard [20] has suggested, that these are all endothelium-lined spaces. He went so far as to state that there are no fibroblasts in tendons and that all the cells are endothelial cells lining spaces for the lubrication of tendons by plasma. His experimental methods are open to several objections, and his observations cannot be regarded as conclusive.

Codman [1h] devised a nomenclature of the structures composing the supraspinatus tendon insertion. The tendon is inserted into the greater tuberosity of the humerus through a layer of fibrocartilage which he called "the palisades." The spindle-shaped cells lying in this layer he named "torpedo cells." A thin calcified layer of this fibrocartilage adjacent to the bone is called the "blue line." This line is formed from about 12 to 18 years of age. The cortical bone beneath the blue line is the "armor plate." The "critical portion" of the supraspinatus tendon is the half-inch (1.3 cm.) proximal to the palisades, so named because it is at this point that rupture occurs.

II. DEGENERATION AND RUPTURE OF THE SUPRASPINATUS TENDON

Historical.—The first to recognize a rupture of the supraspinatus tendon was Smith [21] in 1835. Working on anatomic specimens, some of them "snatched from the grave," he described 7 cases of "injuries" of the shoulder in a series of 40 cadavers. The lesions he described were rupture of the supraspinatus tendon with or without rupture of the other short rotator tendons and sometimes rupture of the long head of the biceps with secondary reattachment in the bicipital groove. He attributed these lesions to dislocation of the head of the humerus. It must be noted, however, that in 1788 Alexander Monro [22] in his "Description of all the 'Bursae Mucosae' of the Human Body" published an illustration of "a hole worn in the capsular ligament of the humerus on the right side." It seems that Monro must be given the credit for first describing a ruptured supraspinatus tendon, even if he did not recognize it as such because of the blending of the tendons of the short rotators of the humerus with each other and with the capsule of the shoulder joint. It was not until 1911 that Codman [1d] recognized rupture of the supraspinatus tendon as a clinical entity. By means of arduous work and many publications and by his book "The Shoulder" he has succeeded in arousing interest in this and other degenerative lesions making up a very important group of conditions affecting the shoulder joint.

Pathologic Anatomy.—Rupture of the supraspinatus tendon occurs as a transverse tear in the fibers of the tendon within a half-inch of the insertion of the tendon into the greater tuberosity of the humerus. The rupture may be partial or complete. Incomplete rupture may occur on the joint side of the tendon where it is called a rim rent, on the bursal side of the tendon involving the floor of the

19. (*a*) Lindblom, K.: Arthrography and Roentgenography in Ruptures of Tendons of the Shoulder, Acta radiol. **20**:548, 1939. (*b*) Rau, cited by Honigsman, F.: Med. Klin. **22**:728, 1926. (*c*) Sobotta, J.: Atlas of Human Histology and Microscopic Anatomy, translated by U. H. Piersol, New York, G. E. Stechert & Company, 1930. (*d*) Lindblom.[10]

20. Howard, N. J.: Pathological Changes Induced in Tendons Through Trauma and Their Accompanying Clinical Phenomena, Am. J. Surg. **51**:689, 1941.

21. Smith, J. S.: Pathological Appearances of Seven Cases of Injury of the Shoulder Joints, with Remarks, Am. J. M. Sc. **16**:219, 1835.

22. Monro, A.: A Description of All the "Bursae Mucosae" of the Human Body, Edinburgh, C. Elliot, T. Kay & Co., 1788.

subacromial bursa or within the substance of the tendon, involving neither surface.[1h] When a rim rent occurs there is apparent lengthening of the tendon.[7b] If the bursal side is first involved there is furring of the floor of the bursa and later fibrillation of the tendon fibers.[23]

In the majority of cases of complete rupture there is found a defect at the critical portion of the supraspinatus tendon which allows free communication between the shoulder joint and the subacromial bursa. Sometimes the rupture extends to the subscapularis or may even involve the latter alone; sometimes it extends to the insertions of the infraspinatus and teres minor tendons, and sometimes it involves all four tendons, thus completely tearing away the lateral margin of the capsule of the shoulder joint.[1h] In some cases there is blood clot in the early stages and in others none.[24] As the defect of the supraspinatus tendon grows older it becomes triangular,[25] making the rent an equilateral triangle with its base on the greater tuberosity and its apex disappearing under the acromion.[26] The apex becomes falciform and is lined by a rim of hyaline tissue.[1h] Sometimes there is a strap of tendon tissue traversing the rent from apex to base.[27] Meyer cited 1 case in which attrition was carried so far that the deltoid muscle as well as the joint capsule was worn away, leaving only skin and fascia to cover the joint.[28]

In cases of recent rupture a stub of the ruptured tendon is attached to the greater tuberosity of the humerus. This stub is gradually worn away.[29] It has been observed to have disappeared in seventy days.[24a] With rupture of long standing there may be found little bony excrescences on the tuberosity. These are thought to be the result of periosteal reaction to minor repeated traumas. Beneath the cortex there may be seen little absorption caverns.[1h] These may also be seen in normal bones and are supposed to be the result of age.[30] Finally the tuberosity is completely worn away (recession),[31] leaving a smoothly rounded area covered with a thin fibrous layer of periosteum,[1h] which continues the rounded contour of the articular head of the humerus. In cases of long-standing rupture, moreover, the articular cartilage of the head of the humerus is eroded.[32] This erosion is slightly larger than the overlying rent because of movement of the humerus.[33] Eburnation of the receding tuberosity and the overlying acromion may also occur.[34]

Another feature noted in cases of long-standing rupture is that the roof of the subacromial bursa, which normally is filmlike, is as thick as blotting paper.[35]

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23. Meyer, A. W.: Further Evidences of Attrition in the Human Body, Am. J. Anat. **34**: 241, 1924.

24. (*a*) Davis, T. W., and Sullivan, J. E.: Rupture of Supraspinatus Tendon, Ann. Surg. **106**:1058, 1937. (*b*) Mayer, L.: Rupture of the Supraspinatus Tendon, J. Bone & Joint Surg. **19**:640, 1937.

25. Codman.[1h] Skinner.[9] Wilson.[4a]

26. (*a*) Keyes, E. L.: Observations on Rupture of Supraspinatus Tendon Based on Study of Seventy-Three Cadavers, Ann. Surg. **97**:849, 1933. (*b*) Codman.[1h]

27. Codman.[1h] Davis and Sullivan.[24a] Keyes.[26]

28. Meyer, A. W.: Chronic Functional Lesions of the Shoulder, Arch. Surg. **35**:646 (Oct.) 1937.

29. Codman.[1h] Skinner.[9]

30. Meyer, A. W.: Unrecognized Occupational Destruction of the Tendon of the Long Head of the Biceps Brachii, Arch. Surg. **2**:130 (Jan.) 1921.

31. (*a*) Horwitz, M. T.: Lesions of the Supraspinatus Tendon and Associated Structures: Investigation of Comparable Lesions in Hip-Joint, Arch. Surg. **38**:990 (June) 1939. (*b*) Codman.[1h] (*c*) Skinner.[9]

32. Codman.[1h] Meyer.[30] Skinner.[9]

33. Keyes, E. L.: Cadaver Observations: Anatomical Observations on Senile Changes in the Shoulder, J. Bone & Joint Surg. **17**:953, 1935. Codman.[1h]

34. Codman.[1h] Meyer.[23] Meyer.[28] Meyer.[30]

35. Codman.[1h] Horwitz.[31]

Synovial villi may be found in the bursa.[36] At operation they are pink, but at autopsy they are limp and colorless. Sometimes thick fibrous bands are found in the bursa.[37] The subacromial bursa may be absent, there being only a loose areolar tissue binding the internal surface of the deltoid to the joint capsule.[23] Roughening, fraying and complete destruction of the synovial bursae may result from long-continued wear,[28] from rupture of the supraspinatus tendon [38] or from a deposit of calcium in the supraspinatus tendon which has ruptured into the bursa.

The tendon of the long head of the biceps muscle is exposed as it passes over the head of the humerus by a rent in the supraspinatus tendon.[39] It is seen as a bright pink [1h] or frayed [29] band crossing the articular cartilage of the humeral head and may sometimes be twice as wide as its natural diameter. In cases of long-standing rupture of the supraspinatus tendon the intra-articular portion of the biceps tendon is absent. The attachment at the supraglenoid tubercle has been lost and the tendon has become reattached in the bicipital groove or to the transverse humeral ligament.[40] The intracapsular portion may disappear completely or may fuse with the joint capsule.[30] It has also been described as being attached to the articular surface of the head of the humerus like a ligamentum teres.[31a] Meyer [28] took great pains to point out that rupture of the biceps tendon occasionally (3 cases) may occur with an intact shoulder capsule, and he attributes this to attrition. His 3 patients had roughening of the head of the humerus. Other causes of rupture of the biceps tendon were adequately discussed by Gilcreest,[39a] but they must be rare.[7b]

Characteristic histologic changes are found in the degenerating but intact supraspinatus tendon.[7b] The tendon bundles lose their wavy appearance and become at first granular, later clear and homogeneous and finally fibrillar. There is an increase in the number of arterioles, and they can be seen growing down from the base of the subacromial bursa and occasionally up from the joint capsule. With hematoxylin and eosin, normal tendon bundles stain a deep pink. The more degenerate a tendon is, the paler pink it will stain. Mallory's connective tissue stain colors the normal tendon bundles orange and the degenerative areas blue. The most marked changes of this character are found in ruptured tendons at the site of rupture. It is evident that the degenerative process described leads to weakening of the tendon of such a degree that eventually rupture of the tendon under relatively slight strain becomes possible.[7b] It has been stated [41] that degenerated areas stain a deeper pink with eosin, but in my series this has not held true.[7b] It is almost impossible to find a histologically normal supraspinatus tendon in an old person.[1h]

At the insertion the torpedo cells may become calcified, may form peculiar giant cells or may fade. The palisades often stain irregularly, indicating necrotic changes. The blue line may be pushed up by excrescences or torn out in patches by the tendons. The armor plate may be at first thickened and later thinned in a receding tuberosity.[1h] There is a thin layer of fibrous tissue covering the bony cortex of the receding tuberosity. Beneath the excrescences are often found caverns con-

36. Codman.[1h] Meyer.[30]

37. Ferguson, L. K.: Painful Shoulder Arising from Lesions of Subacromial Bursa and Supraspinatus Tendon, Ann. Surg. **105**:243, 1937. Codman.[1h]

38. Akerson, I. B., and Codman, E. A.: Pathology Associated with Rupture of the Supraspinatus Tendon, Ann. Surg. **93**:348, 1931.

39. (*a*) Gilcreest, E. L.: The Common Syndrome of Rupture: Dislocation and Elongation of the Long Head of the Biceps Brachii; Analysis of One Hundred Cases, Surg., Gynec. & Obst. **58**:322, 1934. (*b*) Wilson, P. D.: The Painful Shoulder, Brit. M. J. **2**:1261, 1939. (*c*) Codman.[1h] (*d*) Meyer.[30] (*e*) Smith.[21] (*f*) Wilson.[4a]

40. Codman.[1h] Horwitz.[31] Meyer (footnotes 23, 28 and 30). Skinner.[9]

41. Codman.[1h] Lindblom (footnotes 10 and 19 *a*).

taining vascular tissue. In a late stage, when the tuberosity is receding, the blue line tends to disappear. The armor plate may be thickened following rupture but is thin in recession of the tuberosity.[1h] In the subacromial bursa there are vascular and cellular villi which project into the bursa,[42] and in a late stage the walls of the bursa are thickened.

Tensile Strength.—Cronkite,[43] using tendon strips from various tendons with a cross-sectional area of approximately 0.5 to 1 sq. mm., tested the breaking strength and found variations from 4,000 to 30,000 pounds per square inch (2.8 to 21 Kg. per square millimeter) for individual tendons. The average breaking strength of the tendons of different cadavers varied from 8,700 to 18,000 pounds per square inch (6 to 12.5 Kg. per square millimeter). The tensile strength of fresh tendon did not in his estimation differ much from that of tendon fixed with glycerin and alcohol. The strength of the tendons appeared to have no relationship to the assigned cause of death or to the age of the patient. He estimated that a pull of 1,000 pounds (454 Kg.) would be required to rupture a normal supraspinatus tendon 3 mm. thick and 2 cm. wide.

McMaster[44] made preparations of rabbit's gastrocnemius muscle, intact with its tendon and bones of origin and insertion. He subjected the system to strain by pulling the two bones apart in the direction of normal muscle pull. The break in a normal preparation occurred anywhere but in the tendon. The closest approach to a break in the tendon occurred when it pulled away from the calcaneus, carrying a fragment of bone with it. Approximately one half of the tendon's fibers had to be severed to permit rupture of the tendon when the system was subjected to strain. Spontaneous rupture did not occur after severance of three fourths of a tendon's fibers under ordinary activities of a rabbit. This proved that the tendon is the strongest link in this particular muscle to bone chain in the rabbit. Obstruction of the blood supply of 1 cm. of a normal tendon by double ligation caused rupture at the obstructed area, but only when it was subjected to strain four to five weeks later. When tests were made earlier than this the break occurred not in the tendon but elsewhere in the system. The blood supply of a tendon was found to be more important in reparative processes of injured tendons than the presence of a tendon sheath.

Lindblom[45] experimented with preparations of humerus, supraspinatus tendon and muscle with sutures placed in the latter to act as a grip. By exerting a sudden force of 4 to 11 Kg. he was able to produce rupture of the tendon at its insertion in 2 cases out of 7. His conclusion was that the direction of force was important, but since the only persons in which he was able to produce experimental rupture of the supraspinatus tendon were over 70 years of age it would seem, in view of my work,[7b] that these tendons were probably in at least a slightly degenerated state. In younger persons Lindblom did not succeed in producing a rupture in the tendinous portion of the system. In my small series[7b] rupture occurred anywhere but in the tendinous portion of a bone-muscle-tendon-bone preparation of the supraspinatus muscle. The conclusion is that rupture of a normal tendon does not occur and that prior degenerative changes with weakening of the tendon are essential to its rupture by force.

Incidence.—The figures of incidence of complete rupture of the supraspinatus tendon have varied with different authors according to the type and age of the

42. Codman.[1h] Howard.[20]

43. Cronkite, A. E.: Tensile Strength of Human Tendons, Anat. Rec. **64**:173, 1936.

44. McMaster, P. E.: Tendon and Muscle Ruptures: Clinical and Experimental Studies on the Causes and Location of Subcutaneous Ruptures, J. Bone & Joint Surg. **15**:705, 1933.

45. Lindblom (footnotes 10 and 19*a*).

subjects with which they were working. Statistics generally have been given as a percentage of the number of shoulders examined (i. e., two shoulders per subject). Codman,[1h] working on autopsy and surgical material, estimated that the incidence on this basis was at least 5 per cent. Akerson,[38] doing autopsies on old, debilitated people, found it to be 39 per cent. In Skinner's series [9] it was 6 per cent and in Keyes' series 13 per cent.[26a] My own statistics [7b] were quoted as a percentage of the bodies examined, since each case, in a clinical sense, means 1 patient and this is what is important, not whether the rupture is unilateral or bilateral. In autopsy material the incidence was 20 per cent and in anatomic cadavers 26.5 per cent. In about half the cases rupture was bilateral. The average age of the autopsy subjects was 55 years and of the cadavers was 66, but in both groups the average age of those with ruptured tendons was virtually the same. All authors have agreed that the average age of subjects with rupture is in the neighborhood of 64 years.[46] Rupture occurs much more frequently in males than in females, the incidence in my series being 23.7 per cent among males and 17.8 per cent among females.[7b] The incidence is much higher on the right side than on the left,[47] although in one series this was not true.[26a] In my series [7b] no rupture occurred on the left side without a larger one on the right. All unilateral ruptures occurred on the right side except in 2 instances. These were the only cases in the series in which the circumference of the left arm at the level of the biceps exceeded that on the right.

Etiology and Pathogenesis.—Much has been written concerning the cause of rupture of the supraspinatus tendon. Certain general hypotheses are admitted by every one, but no definite proofs have been established. There has been more theorizing than definite data on this subject. Every one agrees that ruptures do not usually occur in persons under the age of 50 years. Actual figures based on the examination of at least 500 bodies bear this out.[48] The youngest patient on record was a woman only 32 years of age.[49] In the younger age groups, instead of rupture of the tendon, fracture of the greater tuberosity occurs. Many authors have speculated that changes occur in the structure of the tendon with age, but the ideas concerning these changes vary, some authors having merely postulated a senile degeneration and gone no further.[50] It has been suggested that degeneration may be due to deterioration of the vascular supply.[51] The supposed change has also been called a sclerosization.[45] Wilson and Duff [7b] have shown that characteristic microscopic degenerative changes make their first appearance relatively early in adult life and increase with age.

Most surgeons are of the opinion that rupture usually occurs in a tendon which has suffered degeneration and then been subjected to trauma.[52] There are divergent opinions as to the nature of this trauma. Most authors believe that the trauma is the result of muscular violence. Smith [21] in his original article expressed the opinion that dislocation of the head of the humerus was the cause, and Outland and Shepherd [53] reported 3 cases in which such dislocation was responsible. It has been pointed out that when external rotation of the humerus

46. Keyes.[26a] Wilson.[7b]

47. Akerson.[38] Lindblom.[10] Wilson.[7b]

48. Codman.[1i] Keyes.[26a] Keyes.[33] Lindblom.[45] Wilson.[7b]

49. (*a*) Fowler, E. B.: Stiff and Painful Shoulders Exclusive of Tuberculosis and Other Infections, J. A. M. A. **101**:2106 (Dec. 20) 1933. (*b*) Thompson, C. E., and McLaughlin, C. W., Jr.: Calcified Deposits in Subscapularis Tendon, Am. J. Surg. **32**:524, 1936.

50. Davis and Sullivan.[24a] Gray.[15a] Horwitz.[31a]

51. (*a*) Codman.[1h,1] (*b*) Wilson.[4a]

52. Codman.[1b,1] Gray.[15a] Horwitz.[31a] Keyes.[26a] Lindblom.[45] Skinner.[9] Wilson.[4a]

53. Outland, T. A., and Shepherd, W. F.: Tears of the Supraspinatus Tendon: Résumé of Twelve Operated Cases, Ann. Surg. **107**:116, 1938.

is prevented during abduction, the coracoacromial arch bears sharply on the insertion of the supraspinatus tendon and may lacerate it.[16] A traumatic condition simulating rupture may occur in a healthy tendon. This has been well illustrated by Codman,[1h] in whose book there is a plate showing a tendon in which the torn end contains a fragment of bone. That this is a traumatic fracture of the greater tuberosity rather than of the tendon is in agreement with experimental results.[54] Howard [20] presented the idea that trauma may cause a vascular granulation tissue reaction which erodes and frays the tendon so that it eventually ruptures under stress. This suggestion was based on his study of the extensor tendons of the finger.

It has also been suggested [55] that rupture is due to wear, caused by long-continued use of the arm in abduction with friction against the coracoacromial arch. Codman described ruptures on the under surface of the tendon and pointed out that these could not very well be due to friction against the acromion.[1h] Meyer granted this but pointed out that complete capsular defects may occur anteriorly and posteriorly to the intact supraspinatus tendon [55] and argued that they cannot be due to trauma but must be due to wear,[28] since some of them are parallel to the tendon fibers instead of transverse as would be the case in traumatic rupture.

Various authors [56] have emphasized the importance of occupation. Most of them cite as the cause of rupture of the supraspinatus tendon occupations which require long-continued use of the arm in a position of abduction, especially doing heavy labor. Codman [1] stated that he had encountered only 1 case of rupture in a person whose occupation did not require or had not required heavy work. Whether occupation causes ischemia, due to compression of the vascular supply,[57] or attrition, because of friction,[55] is still problematic. In my series [7b] the histologic changes of degeneration were greater in laboring people.

Todd and Cohen [58] have found in guinea pigs deprived of vitamin C such weakening of the ligaments that it was difficult to skin the animals without tearing the ligaments of the joints, especially of the knee and cervical vertebrae. It seems doubtful, however, that deficiency of vitamin C could be of great importance in patients showing no other signs of vitamin deficiency.

Clinical Features.—The first clear description of the clinical features in the acute stage of complete rupture of the supraspinatus tendon was given by Codman.[1h] Usually there have been no symptoms in the shoulder prior to the acute disability, which starts with an injury, usually a fall, in which there is sudden elevation of the arm in an attempt to regain balance. The patient will usually say that he fell and struck his shoulder. This may very rarely be true, but usually it is not, and even if the patient did fall on his shoulder he could not have injured the supraspinatus tendon in falling, since it is protected by the acromion process. After the fall, immediate, sharp, brief pain is always felt in the shoulder at the insertion of the supraspinatus muscle. It may be mild or moderately severe, but is usually not severe enough to prevent the patient from working for the remainder of the day. In the evening the pain becomes worse and later in the night intolerable. The patient calls a doctor, or sits up in a chair or walks the floor. All these features are present within twenty-four hours after the injury. Next day he is

54. McMaster,[44] Wilson.[7b]

55. Meyer, footnotes 23, 28 and 30.

56. Codman.[1h,1] Davis and Sullivan.[24a] Keyes.[26a] Meyer.[55] Skinner.[9]

57. Codman.[1h,1]

58. Todd, T. W., and Cohen, M. B., cited by Todd, T. W.: Skeleton and Locomotor System, in Cowdry, E. V.: Problems of Aging, Baltimore, Williams & Wilkins Company, 1939, p. 323.

pretty sure to report that he cannot work but may persuade an accommodating foreman to let him "hang around for a day or two" until he gets better, because he usually thinks that the injury is of no great consequence and will wear off. Physical examination reveals an inability to raise the arm. There is little restriction of movement of the shoulder when the patient is leaning forward from the hips with the arms hanging down. This is really a modification of Dawbarn's sign,[59] i. e., disappearance of pain when the arm is abducted because the ruptured tendon has slipped up under the coracoacromial arch where it is protected. A tender point can be felt just anterior to the edge of the tip of the acromion process when the arm is in dorsal flexion. This point is at the gap between the torn ends of the tendon. As the arm is passively elevated this tender point disappears under the coracoacromial arch and the patient experiences a sense of relief. Sometimes this gap can be felt as a sulcus by the examining finger if the intervening deltoid muscle is not too thick. This sulcus accentuates the prominence of the greater tuberosity. The passage of the sulcus in the ruptured tendon under the coracoacromial arch causes a wince of pain, and a jog which is noticeable to the patient and sometimes even to the examiner. When the symptoms and signs are definite and typical and the sulcus is plainly palpable, there should be no doubt of complete rupture but in cases of partial rupture each symptom may be milder and each sign somewhat more doubtful than in the cases of complete rupture. The doubtful character of the findings combined with the presence of a considerable amount of power to hold the arm in the scarecrow position (right-angled abduction) rules out a complete rupture.

During the first few nights following a complete rupture the pain is very severe; then it becomes a nagging pain, bearable but very annoying. This pain is felt near the insertion of the deltoid. It continues without change for months and is aggravated by attempts to work.[1h] The spinatus muscles begin to atrophy after about three weeks.[1h] Unless operated on, the patient never completely recovers the use of his arm. Codman stated that some courageous men persist in working and become free of symptoms in two to five years.[1h] In a late stage there is no tender point, jog or wince. Because of the relatively large number of ruptures found at autopsy, Keyes [26a] doubted that all of them cause symptoms.

Partial rupture may cause pain and disability for a short period and then become symptomless or may go on to adhesions and a "frozen shoulder." [37] In the latter condition slight abduction is painless but cannot be carried beyond this point. This is part of the so-called "subacromial bursitis."

Rupture of the long head of the biceps tendon is one end result of complete rupture of the supraspinatus tendon.[60] When rupture occurs the symptoms are variable.[39a] There may be pain, a sudden, loud perceptible snap or both, or only weakness of the arm. Objectively there may be a bulge of contracted biceps muscle, depending on whether or not secondary reattachment of the tendon has previously occurred in the bicipital groove. A partially torn biceps tendon may give rise to more pain through irritating its sheath by friction than does a completely ruptured tendon.[39a] This point is illustrated in a case described by Moseley [14] of a man with a complete rupture of the supraspinatus tendon which was operated on. Ten years previously he had "the same injury" to the other shoulder, which remained painful for two years until one day he felt a sudden snap in the shoulder and

59. Dawbarn, R. H. M.: Subdeltoid Bursitis: A Pathognomonic Sign for Its Recognition, Boston M. & S. J. **154**:691, 1906.

60. (*a*) McKee, G. K.: Spontaneous Rupture of the Long Head of the Biceps, Brit. M. J. **1**:1018, 1940. (*b*) Meyer.[30] (*c*) Moseley.[14]

noted a swelling of his biceps muscle, after which his shoulder was free of pain. The tendon may be displaced instead of ruptured if the lesser tuberosity is worn away.[30]

The rupture of the tendon of the long head of the biceps muscle is most often caused by friction resulting from a capsular defect,[61] i. e., a rupture of the supraspinatus tendon and erosion of the articular cartilage of the head of the humerus.[39b] Secondary reattachment of the ruptured tendon to the bicipital groove or the transverse humeral ligament usually occurs before complete severance of the biceps tendon, because some of the severed and reattached tendons are of the same length as normal tendons.[62] Sometimes, however, rupture occurs before the secondary reattachment, and the tendon is longer than normal and hence functionally useless.

There are two roentgenographic methods for determining whether a supraspinatus tendon is ruptured. Henry[63] employed soft tissue roentgenographic technic using anteroposterior views with the arm in adduction and internal rotation. Immediately after the injury, fine spicules of bone may be seen near or on the periosteal outlines of the greater tuberosity at the site of insertion of the supraspinatus tendon in those cases in which the tendon has been torn off the greater tuberosity.[63] Usually, however, the rupture occurs at the critical portion of the tendon, and in these cases the roentgenogram appears normal. The humeral head is held high in the glenoid cavity.[18a] Within several weeks after the injury the density of the bone of the greater tuberosity varies from the normal; atrophy of the trabeculae or irregular roughening about the sulcus occurs[63] (osteitis of Codman).[1h] Within six months to one year there are found rounding off and loss of the greater tuberosity, irregular calcification and occasionally cysts in the cortical bone of the head of the humerus. Older lesions may also show thickening of the cortex (eburnation of Codman) and rearrangement of the trabeculae.[63]

Lindblom[19a] introduced the method of injecting a solution of 6 cc. of a 35 per cent solution of diodrast mixed with 1 cc. of 1 per cent procaine hydrochloride solution into the shoulder joint 1 cm. anterolateral to the coracoacromial joint, in the direction of the center of the head of the humerus. The arm is moved passively to spread the contrast medium, and roentgenograms are taken immediately, because the solution is rapidly absorbed. Normally the contrast medium fills the cavity of the joint, the tendon sheath of the biceps and the bursa of the subscapularis muscle. No other communications exist in the normal joint except an occasional communication with a bursa very rarely found under the infraspinatus tendon.[3a] In cases of rupture of the supraspinatus tendon, either a finger-like projection flows out of the joint cavity or else a free communication exists between the joint and the subacromial bursa.

Treatment.—Credit for the present knowledge of the treatment of complete rupture of the supraspinatus tendon must go to Codman. The treatment is operative repair, and the best time is immediately after the injury.[64] When the diagnosis was doubtful Codman advised exploratory incision of the bursa with local anesthesia.

61. McKee.[60a] Meyer.[30] Wilson.[39b]

62. Meyer (footnotes 28 and 30).

63. Henry, L. S.: Roentgenographic Evidence in the Tuberosity of the Humerus of Recent and Old Injuries to the Supraspinatus Tendon Attachment, Am. J. Roentgenol. **33**:486, 1935.

64. Brumbaugh, H. L.: (*a*) Rupture of Supraspinatus: Diagnosis and Treatment of Post-Traumatic Changes in and About Joints, Ohio State M. J. **35**:597, 1939; (*b*) Calcifying Tendinitis Traumatica, Am. J. Surg. **48**:681, 1940. (*c*) De Courcy, J. L.: Rupture of Muscles and Tendons, Am. J. Surg. **36**:283, 1937. (*d*) Codman.[1d, f, g, h, i] (*e*) Davis.[24a] (*f*) Gray.[15a] Laird.[8] McKeown.[7a] Moseley.[14] Moseley.[6] Moseley.[18a] Wilson.[4a] Wilson.[39b]

The position of the patient during operation is important.[1h] The requirements are that the shoulder must be held steady yet the position must permit mobilization of the arm to allow all the short rotator tendons of the shoulder to be visualized through the small operative incision, as the arm is rotated. Codman's position fulfils these requirements. A heavy sandbag is placed under the affected shoulder and another under the hip on the same side, thus turning the patient partly on his side with the head and neck falling away from the operative field. The patient is placed with the affected shoulder at the side of the table, so that the affected arm hangs over the edge to permit its rotation by an assistant. The whole arm is draped so that it can be handled.

A vertical incision 1½ inches (3.8 cm.) long is made over the anterior aspect of the head of the humerus with its upper end near the acromioclavicular joint and its lower end at the top of the bicipital groove.[1h] The latter point is the most anterior prominence when the forearm is flexed to a right angle to the arm and placed at a right angle to the table. This position is important too for incising the bursa, because if the arm is not in this position it is liable to be internally rotated, and then the incision will miss the bursa completely. After the skin and muscle are incised hemostasis should be secured before the bursa is entered. The latter is opened by a method similar to that employed for opening the peritoneum, i. e. by incision between two forceps.

When the bursa has been opened, the arm is rotated to visualize all of the base of the bursa, and the degree of rupture is then easily ascertained. In an early stage (i. e., within two weeks [24a]) repair is easy. In a late stage, in which retraction of the tendon has occurred, it is difficult. The tendon should be mobilized as much as possible and then pulled down. Injury to the suprascapular nerve as it winds around the lateral border of the spine of the scapula must be avoided. Sutures will tear out of the hyaline edge of the falciform border of an old defect; so this edge must be pared away before repair is attempted. If the long head of the biceps tendon is roughened and not capable of forming a smooth cord, it should be divided and the lower end attached to the bicipital groove and the upper portion attached to the supraspinatus tendon so as to help fill the gap. If the biceps tendon is intact it should be left alone, so that its function of stabilizing the shoulder may remain. The other functions of the biceps tendon are maintained when the long head has been sutured to the bicipital groove.

Heavy silk is probably the best material to use for repair of the defect in the tendon,[1] but fascia lata has also been employed. If there is no stub of tendon on the greater tuberosity capable of holding sutures, holes should be bored in the greater tuberosity, through which the heavy silk sutures may be passed. Soon after the rupture the closure of the defect is simple; in a later stage, when there is retraction of the tendon it may be necessary also to close the defect from side to side. To give the tendon a surface to adhere to, the tuberosity should be roughened,[1h] or even a little slot cut as a new sulcus to which the tendon is held.[65] The roof of the subacromial bursa should be left open to permit the escape of fluid which if confined would cause pain.[1h] Very rarely persistent pain after the operation may be due to reaction of the tissues about the silk sutures. This can be relieved by opening the bursa with local anesthesia and removing the sutures.

The saber cut incision dividing the acromion, while giving a better exposure, converts a minor into a major surgical operation,[1h] and Codman abandoned it. It may be useful in cases of old rupture when the surgeon requires a greater exposure. P. D. Wilson makes the 1½ inch (3.8 cm.) anterior incision, and if

65. Wilson.[4a] Wilson.[39b]

the rupture is found to be very large he then makes the saber cut incision.[4a] Codman found that with an able assistant to rotate the arm adequate exposure was supplied by the small anterior incision through the deltoid muscle. There is little to support Mayer's contention [24b] that this incision weakens the fibers of the deltoid muscle anterior to the incision unless, of course, one cuts so low as to divide the circumflex nerve.

Regarding the problem of postoperative treatment, there are advocates of both abduction and adduction positions. Codman [1] recommended a pad in the axilla and a small pillow for the arm and forearm to prevent too much internal rotation. After the first night the patient is allowed to assume any position which he finds comfortable. The patient is given gradually increasing exercise, at first using passive movement by bending at the hips and letting the arms hang down, so that by the end of a week he can bend the hips to a right angle. By gently twisting and rolling the shoulder he can move it passively. During the second week he should start swinging the arms actively in the bent-over position. He may be discharged in ten to fourteen days to continue the stooping exercises until he can abduct the arm freely and then should start abduction in the erect position. Others have advised immobilization in 60 degrees of abduction for two or three weeks after operation [66] and even in 120 degrees for four weeks.[24b] This procedure causes an abduction contracture, which, however, will yield in several weeks.[24b] If any one elects to use abduction he should be certain to remember that the abducted arm should be slightly anterior to the coronal plane of the body, i. e., in the plane of the scapula.

One method of treatment of partial rupture is to maintain a complete range of movement from the beginning.[67] In the early treatment injection of procaine hydrochloride into the most tender spot relieves the pain, and the movements can then be carried out.[18a] Short wave diathermy is also of use.[68] The other method of treatment is by immobilization, application of heat and gradually increasing exercises within the limit of pain.[37] Operation offers these patients nothing.[1b]

If there is rupture of the tendon of the long head of the biceps associated with an old complete rupture of the supraspinatus tendon, nothing can be done for the latter at this late stage, but the biceps tendon should be sutured to the bicipital groove or to the short head of the biceps muscle, the coracoid process or both.[69] For slight tears of the biceps tendon the arm may be immobilized without operation in acute flexion for two or three weeks. It is then gradually lowered and physical therapy started. This method reduces the muscular power of the biceps by about 30 per cent, and the cosmetic effect is poor.[60a] McKee [60a] makes the incision for repair of a rupture of the supraspinatus tendon also a lower one, over the biceps tendon, below the insertion of the pectoralis major muscle. He threads the tendon back through its groove and sutures it in the intertubercular sulcus below the notch.

III. CALCIFICATION OF THE SUPRASPINATUS TENDON

Historical Aspects.—Painter in 1905 [70] was the first to recognize calcium deposits in roentgenograms of the shoulder. He thought the shadows he observed were due to thickening of the subdeltoid bursa. But Codman, who was present

66. Davis and Sullivan.[24a] Moseley.[6]

67. Codman.[1b] Moseley.[6] Moseley.[14] Moseley.[18a]

68. Moseley (footnotes 6, 14 and 18 *a*).

69. Bishop, W. A., Jr.: Calcification of the Supraspinatus Tendon: Cause, Pathologic Picture and Relation to Scalenus Anticus Syndrome, Arch. Surg. **39**:231 (Aug.) 1939.

70. Painter, C. F.: Subdeltoid Bursitis, Boston M. & S. J. **156**:345, 1907.

at one of Painter's operations, was the first to realize that the deposit was actually in the supraspinatus tendon.

Pathologic Anatomy.—Gross: Calcium is deposited in the short tendons of the shoulder capsule,[71] most frequently in the supraspinatus tendon.[72] On the base of the subacromial bursa in the tendon involved there is an elevation with a grayish white center and a red turgid periphery, resembling a boil.[73] The bursa contains a fibrinous exudate. The calcium deposit at this stage is soft and creamy[74] and resembles staphylococcic pus or may be firmer and of the consistency of toothpaste. The areas of deposit are frequently multiloculated.[18a] The acute symptoms are caused by involvement of the base of the subacromial bursa.[75] The calcium deposit may rupture into the subacromial bursa, producing a chemical bursitis,[76] and the site of rupture may often be demonstrated at operation.[77]

In the subacute and chronic phases there is usually little abnormality to be seen in the bursa. The deposit may have to be located by feeling a swelling.[78] The deposit is usually cheesy or gritty.[79] In some cases it will shell out easily, but in others it is embedded among the fibers of the tendon,[80] requiring curettage.

Microscopic: Calcium deposits may occur as a number of foci of varying size embedded in a tendon which shows fibrosis and is infiltrated with masses of chronic inflammatory cells, mostly lymphocytes and plasma cells with a few giant cells. The connective tissue may show hyalinization.[81] In a case I studied recently the tendon contained many polymorphonuclear leukocytes as well as small round cells and giant cells.

Chemical Composition of the Deposits.—Calcium has been reported as occurring in the form of calcium carbonate and calcium phosphate ($Ca_3[PO_4]_2$),[82] and some analyses show calcium oxalate.[83] The analyses have differed greatly as to the proportion in which these calcium salts occur.

Incidence.—The only reliable figures of incidence are those of Bosworth.[71a] Among 6,061 supposedly normal persons of the "white collar" class, calcium was found on routine fluoroscopic examination in 165 (2.7 per cent) in one or both shoulders. The lesion was found most frequently in the period of greatest activity

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71. (*a*) Bosworth, B. M.: Calcium Deposits in Shoulder and Subacromial Bursitis: A Survey of 12,122 Shoulders, J. A. M. A. **116**:2477 (May 31) 1941. (*b*) Brickner, W. M.: Prevalent Fallacies Concerning Subacromial Bursitis: Its Pathogenesis and Rational Operative Treatment, Am. J. M. Sc. **149**:351, 1915. (*c*) Carnett, J. B.: Calcareous Deposits of the So-Called Subacromial Bursitis, Surg., Gynec. & Obst. **41**:404, 1925. (*d*) Emslie, R. C.: Calcareous Deposits in the Supraspinatus Tendon, Brit. J. Surg. **20**:190, 1932. (*e*) Fahey, J. J., and Harmon, P. H.: Calcification of Posterior Portion of the Greater Tubercle of the Humerus: Differentiation from Supraspinatus Tendon Calcification, Am. J. Roentgenol. **38**: 707, 1937. (*f*) Rogers, M. H.: Treatment of Subdeltoid Bursitis, Am. J. Surg. **43**:292, 1939. (*g*) Wardle, E. N.: Calcification in Supraspinatus Tendon, J. Bone & Joint Surg. **17**:789, 1935. (*h*) Codman.[1h] (*i*) Wilson.[4a] (*j*) Wilson.[39b]

72. Bishop.[69] Bosworth.[71a] Codman.[1h]

73. Codman.[1h] Emslie.[71d]

74. Codman.[1h] Rogers.[71f]

75. Codman.[1h] Wilson.[39b]

76. Bishop.[69] Codman.[1h] Moseley.[18a] Wilson.[39b]

77. Brickner.[71b] Wilson.[39b]

78. Codman.[1h] Emslie.[71d]

79. Codman.[1h] Moseley.[18a] Rogers.[71f]

80. Brickner.[71b] Codman.[1h] Rogers.[71f]

81. (*a*) Moschowitz, E.: Histopathology of Calcification of the Supraspinatus Tendon as Associated with Subacromial Bursitis, Am. J. M. Sc. **150**:115, 1915. (*b*) Bishop.[69] (*c*) Codman.[1h] (*d*) Emslie.[71d]

82. Bishop.[69] Brickner.[71b] Emslie.[71d] Moseley.[18a] Painter.[70] Rogers.[71f] Wilson.[39b]

83. Bishop.[69] Brickner.[71b]

of adult life, nearly all of his subjects being under 50 years of age. This has been corroborated by other authors.[84] It occurs more often in males.[85] Among 1,178 males in Bosworth's series,[71a] the incidence of calcification was 3.6 per cent, while among 3,883 females the incidence was only 2.5 per cent.

Etiology and Pathogenesis.—Occupation: Women typists have a significantly higher incidence of calcium deposits than women clerks throughout all age groups.[71a] "Millions of years of heredity have not yet prepared the modern stenographer or machine operator to keep their supraspinatus tendons stretched and under tension, on the qui vive, hour after hour, day after day."[1h] That is to say, long-continued use of the arm in abduction seems to be a predisposing factor.

Trauma: A single severe trauma does not cause calcification but may precipitate acute symptoms in an already existing deposit.[86] Many patients have had known calcium deposits in one or both shoulders for months or years prior to an acute attack,[87] and many patients experience a severe attack with no history of trauma.[88] Many authors have expressed the opinion that minor, often repeated traumas cause necrosis and/or hyalinization due to poor blood supply and that calcification subsequently occurs.[89] This last would seem to be the most likely cause of calcification. A later trauma probably initiates the clinical syndrome.

Infection seems to play no part in the formation of calcium deposits.[90] Many have operated on these deposits and made bacteriologic cultures which have given negative results.[91] Brickner[71b] reported 3 positive results of cultures and Codman and Harrington[1h] 1 culture that yielded Staphylococcus aureus. It was later admitted that the last one was probably contaminated.[1h] Dickson and Crosby[92] expressed the belief that an infectious or toxic focus anywhere in the body may aid in precipitating an attack, but others with wide experience have not agreed with this view.[93] To explain why calcification occurs, Wells's[94] theory of calcification has been invoked.[69] It presupposes the presence of a necrotic area. In such an area no oxidation occurs. Consequently no carbon dioxide is produced and the medium becomes alkaline, causing precipitation of calcium. Calcium values in the blood of persons with large deposits of calcium in the supraspinatus tendon, some with acute symptoms and others without any symptoms, all were normal.[71a]

Clinical Features.—A calcium deposit may be present in one of the tendons of the short rotator cuff without any symptoms, or it may give rise to chronic or acute

84. (*a*) Dick, G. F.; Hunt, L. W., and Ferry, J. L.: Calcification of the Supraspinatus Tendon: New Treatment, J. A. M. A. **116**:1202 (March 22) 1941. (*b*) Bishop.[69]

85. Bosworth.[71a] Wilson.[39b]

86. Bishop.[69] Bosworth.[71a] Carnett.[71c] Codman.[1h] Emslie.[71d] Thompson and McLaughlin.[49b]

87. Bishop.[69] Bosworth.[71a] Carnett.[71c] Codman.[1h] Dick, Hunt and Ferry.[84a] Emslie.[71d] Wilson.[39b]

88. Bosworth.[71a] Codman.[1h]

89. Bishop.[69] Brickner.[71b] Carnett.[71c] Codman.[1h] Dick, Hunt and Ferry.[84a]

90. (*a*) Patterson, R. L., Jr., and Darrach, W.: Treatment of Acute Bursitis by Needle Irrigation, J. Bone & Joint Surg. **19**:993, 1937. (*b*) Bishop.[69] (*c*) Bosworth.[71a] (*d*) Codman.[1h]

91. Carnett.[71c] Dick, Hunt and Ferry.[84a] Emslie.[71d] Wilson.[4a]

92. Dickson, J. A., and Crosby, E. H.: Periarthritis of the Shoulder: Analysis of Two Hundred Cases, J. A. M. A. **99**:2252 (Dec. 31) 1932.

93. Bishop.[69] Bosworth.[71a] Codman.[1h] Patterson and Darrach.[90a] Wilson.[39b]

94. Wells, H. G.: Chemical Pathology, ed. 5, Philadelphia, W. B. Saunders Company, 1925, pp. 489-496.

symptoms. The latter may occur suddenly or be superimposed on the former.[95] Calcium deposition in a tendon, noticeable in a roentgenogram may develop rapidly, within two months.[71a] The deposit may immediately give rise to symptoms or may slowly increase in size for years (seven years in one case) with perhaps only slight symptoms.[71a] Schujenioff[96] has found calcium deposition in muscles thirty-six hours after suture. Small deposits may occur and disappear without ever causing symptoms, but a very large one (1.5 cm. in profile) will give rise to symptoms before disappearing.[71a] By means of roentgenograms calcium deposits have been observed to disappear with and without treatment.[85] The deposits are temporary and leave no residual roentgen changes. Perhaps some of the tendon defects seen at autopsy result from absorbed calcium deposits.[1h] An acutely inflamed deposit may rupture into the subacromial bursa, setting up a bursitis.[39b] This may perhaps explain the acute attacks in which there is rapid recovery without treatment.[1h]

Acute Phase: An acute attack may appear without warning, often during sleep[97] or during the course of a subacute or chronic attack.[98] There is excruciating pain on any movement of the arm. This pain is felt over the bursa and over the insertion of the deltoid muscle. The deltoid muscle exhibits reflex spasm,[99] which causes limitation of movement. Voluntary fixation eventually leads to actual contracture with limitation of movement from this cause.[69] There is tenderness over the deposit which can be definitely marked out,[100] and in very acute attacks there may be tenderness over the insertion of the deltoid.[101] Atrophy of the spinatus muscles occurs if the symptoms last more than a few weeks.[102] In the acute stage there may be slight fever[103] and leukocytosis.[104] A lump may be felt just medial to the greater tuberosity if the deposit occurs in the supraspinatus tendon.[1h] If untreated, the acute phase may last for several weeks and then revert to a chronic type, may form adhesions or may clear up rapidly if the deposit ruptures into the subacromial bursa.[1h]

Chronic Phase: The onset is insidious. First there is an uncomfortable feeling around the shoulder; later it is hard to find a comfortable position in which to rest the arm at night during elevation of the arm in the coronal plane.[105] Pain is most often felt at the fibers of insertion of the deltoid muscle,[106] while the maximum point of tenderness is over the deposit in the tendon[107]; this is most often close to the greater tuberosity, since most of the deposits occur in the supraspinatus tendon. If there has been a long painful period the whole area becomes sensitive,

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95. (*a*) Bosworth, B. M.: Examination of the Shoulder for Calcium Deposits: Technique of Fluoroscopy and Spot Film Roentgenography, J. Bone & Joint Surg. **23**:567, 1941. (*b*) Bishop.[69] Bosworth.[71a] Carnett.[71c] Codman.[1h] Dick, Hunt and Ferry.[84a] Emslie.[71d] Painter.[70] Wilson.[39b]

96. Schujenioff, cited by Harbin[98a] and Moschowitz.[81a]

97. Bosworth.[71a] Codman.[1h] Wilson.[39b]

98. (*a*) Harbin, M.: Deposition of Calcium Salts in the Tendon of the Supraspinatus Muscle, Arch. Surg. **18**:1491 (April) 1929. (*b*) Bishop.[69] (*c*) Bosworth.[71a] (*d*) Carnett.[71c] (*e*) Codman.[1h] (*f*) Emslie.[71d] (*g*) Wilson.[39b]

99. Bishop.[69] Codman.[1h]

100. Carnett.[71c] Codman.[1h] Emslie.[71d] Painter.[70] Thompson and McLaughlin.[49b]

101. Carnett.[71c] Codman.[1h] Emslie.[71d]

102. Codman.[1h] Dick, Hunt and Ferry.[84a]

103. Dick, Hunt and Ferry.[84a] Patterson and Darrach.[90a] Thompson and McLaughlin.[49b] Wilson.[39b]

104. Dick, Hunt and Ferry.[84a] Patterson and Darrach.[90a] Wilson.[39b]

105. Bishop.[69] Bosworth.[71a] Carnett.[71c] Codman.[1h] Dick, Hunt and Ferry.[84a] Emslie.[71d] Harbin.[98a] Painter.[70] Wilson (footnotes 4 *a* and 39 *b*).

106. Carnett.[71c] Codman.[1h] Emslie.[71d] Patterson and Darrach.[90a]

107. Carnett.[71c] Codman.[1h] Emslie.[71d] Thompson and McLaughlin.[49b]

with pains shooting up into the neck and down to the hand.[108] This has given rise to the misnomer "brachial neuritis." In some cases the hand may swell and the skin becomes atrophic.[109] There may be a certain amount of spasm and limitation of abduction and external rotation at this point.[110] Acute exacerbations may occur at any time during the chronic course.

Roentgen Examination.—Fluoroscopy should be employed and spot roentgenograms taken.[111] The deposit must be seen in profile, or it will be obscured by the underlying bone.[112] Pieces of lead inserted in the tendon were shown to be superimposed on the underlying bone in many positions of the arm, demonstrating the need for fluoroscopic examination.[69] Deposits may be single or multiple [71b] and, if liquid, may be seen to change their shape with movement.[71d] Sometimes at operation a milky fluid containing calcium is found in the bursa which did not show up on roentgen examination.[71a]

Treatment.—Acute Stage: The best treatment of the acute attack is prompt excision of the deposit.[113] In experienced hands it is a relatively minor procedure which gives immediate, certain and complete relief. Local or general anesthesia may be used.[88] The average stay in the hospital is four days,[114] and the patient can return to work with unrestricted motion of the shoulder in three weeks.[71a] The same incision is used as has been described for exposure of a ruptured supraspinatus tendon. Heat is a valuable adjuvant and should be applied locally after operation to speed recovery.[115] Postoperatively only a sling is used.[116]

Irrigation by the two needle method of Patterson and Darrach [90a] has been advocated for acute attacks.[117] It is an operative procedure, and, while good results have been reported by those who favor the method, it is not very satisfactory for solid calcium. The results are not positive, and the deposit, especially if it is a multiloculated one, may easily be missed.[118]

Chronic Stage: The efficacy of treatment of chronic forms is difficult to evaluate, because the patient will get better whatever line of treatment is followed,[88] and even with maltreatment the symptoms will eventually disappear within, at the most, two years.[1h] Removal of the calcium by operation gives the most satisfactory result, although recovery is slower than in the case of an acute deposit.[119] The use of an overhead pulley aids in regaining abduction. If the choice is left to the patients, the majority will elect some form of heat therapy, and over a period of time they will recover.[71a] Under treatment with diathermy [120] the deposits disappear in two and one-half to eleven weeks,[120a] but the patient endures intense pain for a week

108. Carnett.[71c] Codman.[1h] Painter.[70]
109. Bishop.[69] Codman.[1h]
110. Bishop.[69] Codman.[1h] Emslie.[71d] Painter.[70]
111. Bishop.[69] Bosworth (footnotes 71 *a* and 95 *a*).
112. Bishop.[69] Bosworth (footnotes 71 *a* and 95 *a*). Codman.[1h] Dick, Hunt and Ferry.[84a] Emslie.[71d]
113. (*a*) Hitzrot, J. M.: Surgical Diseases of the Shoulder Bursae, Ann. Surg. **98**:273, 1933. (*b*) Bosworth.[71a] Codman.[1h] Moseley.[18a]
114. Bosworth.[71a] Brickner.[71b] Codman.[1h] Emslie.[71d] Painter.[70] Rogers.[71f] Thompson and McLaughlin.[49b] Wilson.[39b]
115. Bosworth.[71a] Moseley.[18a] Painter.[70]
116. Carnett.[71c] Codman.[1h]
117. Bishop.[69] Patterson and Darrach.[90a] Wilson.[39b]
118. Bosworth.[71a] Moseley.[18a]
119. Carnett.[71c] Emslie.[71d]
120. (*a*) Troedsson, B. S.: Diathermy for Calcium Deposits Around Subacromial Bursa and Supraspinatus Tendon, Arch. Phys. Therapy **19**:166, 1938. (*b*) Nilssen, L.: Results of Various Methods of Treatment of Peritendinitis Calcificans of Shoulder Region, Med. rev., Bergen **51**:67, 1934; cited by Troedsson.

or so. The increased vascularity and resulting high carbon dioxide content of the tissue caused by diathermy [64b] makes the medium acid, so that calcium is absorbed. The use of immobilization in abduction causes adhesions and is mentioned only to be condemned.[71a]

IV. SUBACROMIAL BURSITIS

This subject must be included because the subacromial bursa is so frequently involved by lesions affecting primarily the tendons of the short rotators of the shoulder. Subacromial bursitis never arises as a primary condition. The bursa is a limiting structure which is involved only by lesions in the surrounding structures.[121] Codman [1h] and Wilson [39b] believed that the bursa is more sensitive to pain than the surrounding structures. Calcification or rupture of the supraspinatus tendon gives rise to a bursitis.[122] These have been adequately considered in the preceding sections of this review. Tuberculosis of the subacromial bursa has been described but rarely.[123]

It is with trepidation that the last entity is introduced. It is the so-called "periarthritis" or "tendinitis" or "frozen shoulder." This is a condition in which physical examination fails to reveal any swelling or definite point of local tenderness, although there may be definite sensitiveness about the shoulder. There is limitation of both passive and active abduction. If the shoulder girdle is fixed, abduction will not exceed 35 to 45 degrees. If movement is forced, pain is elicited.[124] When the condition is treated by abduction, as advocated by Sir Robert Jones, loud snapping sounds are heard, followed by complete freeing of the movements of the shoulder.[75] If the bursa is opened the results are disappointing. There may be adhesions in the bursa, but usually there are none. With the finger on the base of the bursa, the snapping of adhesions in the tendinocapsular structure beneath the finger may be felt as the arm is manipulated.[75] Codman [1h] and Wilson [39b] both have reported occasionally finding the base of the bursa reddened, and they both felt that this represented the onset of the condition. It may also arise as a sequel of rupture or calcification of the supraspinatus tendon.[39b] The onset of the condition is gradual over the course of several months.

In the treatment of the so-called "frozen shoulder," many authors,[125] using different methods, have reported good results. Given time, two years at the very most, and no treatment at all, the condition will clear up by itself.[1h] Time is the element common to all methods of treatment.[18a] However, good treatment will cut down the amount of time required.[1h] Mild forms will clear up with massage, heat and exercise.[126] The simplest and most effective treatment for the completely frozen shoulder is the hyperabduction treatment of Codman.[1h] The patient is put to bed, the forearm splinted and the splint tied to the head of the bed, which is raised by blocks under the legs if necessary to secure sufficient extension. A small dose of morphine may be given to secure relaxation but not enough to remove pain entirely. In twelve to twenty-four hours the spasm, which contributes to the symptoms, yields, the adhesions give, the greater tuberosity passes under the acromion and the arm becomes abducted and externally rotated. In a day or two the splint is removed and a bandage is tied loosely around the wrist to the head of the bed. The patient gets up daily and carries out exercises bending forward from the hips and letting

121. Codman.[1h] Moseley.[18a] Rogers.[71f] Wilson.[39b]
122. Brickner.[71b] Codman.[1h] Ferguson.[37] Moseley.[18a] Rogers.[71f] Wilson.[39b]
123. Brickner.[71b] Hitzrot.[113a]
124. Codman.[1h] Ferguson.[37] Rogers.[71f] Wilson.[39b]
125. Codman.[1h] Ferguson.[37] Moseley.[18a] Rogers.[71f] Wilson.[39b]
126. Codman.[1h] Rogers.[71f] Wilson.[39b]

the arms hang down. The patient stays in the hospital until he can move the arm about in any direction over the head, usually one or two weeks. For a few weeks after discharge he takes stooping exercises and sleeps with his arm in an abducted position. Wilson [39b] also uses a modified form of the hyperabduction method. Heat (diathermy, electric pad or fomentations) may be of some help.[127] Should the patient not wish to go to bed the manipulation method of Moseley [18a] will give good results for the completely frozen shoulder in a little longer time than the recumbent hyperabduction method. In the case of a shoulder involved to a lesser degree it is probably the method of choice. The area of the subacromial bursa is infiltrated with 50 cc. of 1 per cent solution of procaine hydrochloride, and the shoulder is then manipulated, if possible, through its complete range of movement. Manipulation is followed by twenty minutes of diathermy treatment. The treatment is repeated at intervals until the normal range of painless movement is regained.

127. Codman.[1h] Moseley.[18a] Rogers.[71f]

EFFECTS OF ADMINISTRATION OF SODIUM SULFADIAZINE TO DOGS

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Changes attributed to sulfonamide compounds have been reported by other investigators.[1] We [2] recently reported lesions in dogs produced by sodium sulfadiazine (the monohydrate sodium salt of 2-[paraaminobenzenesulfonamido]-pyrimidine), and similar lesions in the kidney of man have been recorded.[3]

From the Departments of Surgery and Pathology of the New York Hospital and the Cornell University Medical College.

1. (*a*) Molitor, H., and Robinson, H.: Some Pharmacological and Toxicological Properties of Sulfanilamide and Benzylsulfanilamide, J. Pharmacol. & Exper. Therap. **65**:405-423, 1939. (*b*) Antopol, W., and Robinson, H.: Urolithiasis and Renal Pathology After Oral Administration of 2(Sulfanilylamino) Pyridine (Sulfapyridine), Proc. Soc. Exper. Biol. & Med. **40**: 428-430, 1939; (*c*) Pathologic and Histologic Changes Following Oral Administration of Sulfapyridine, Arch. Path. **29**:67-76 (Jan.) 1940. (*d*) Antopol, W.; Lehr, D.; Churg, J., and Sprinz, H.: Changes in the Urinary Tract and Other Organs After the Administration of Three Sulfanilamide Derivatives, ibid. **31**:592-602 (May) 1941. (*e*) Lehr, D., and Antopol, W.: Toxicity of Sulfadiazine and Acetyl Sulfadiazine in Albino Rats with Special Reference to Renal Lesions and Their Significance, Urol. & Cutan. Rev. **45**:545-554, 1941. (*f*) Rake, G.; van Dyke, H., and Corwin, W.: Pathological Changes Following Prolonged Administration of Sulfathiazole and Sulfapyridine, Am. J. M. Sc. **200**:353-362, 1940. (*g*) Toomey, J. A.: Urinary Concretions and Sulfapyridine, J. A. M. A. **113**:250-251 (July 15) 1939. (*h*) Toomey, J. A.; Reichle, H. S., and Takacs, W. S.: Effects on Monkeys of Sulfapyridine in Doses Comparable with Those Used for Infants, J. Pediat. **16**:179-190, 1940. (*i*) Climenko, D. R., and Wright, A. W.: Effects of Continued Administration of Sulfathiazole and Sulfapyridine in Monkeys, Arch. Path. **32**:794-817 (Nov.) 1941. (*j*) Climenko, D. R.; Barlow, O. W., and Wright, A. W.: Influence of Sodium Bicarbonate in Preventing Renal Lesions from Massive Doses of Sulfathiazole, ibid. **32**:889-894 (Dec.) 1941. (*k*) Gross, P.; Cooper, F. B., and Hagan, M. L.: Urolithiasis Medicamentosa Caused by Sulfadiazine, Am. J. Clin. Path. **11**:882-889, 1941. (*l*) French, A. J., and Weller, C. V.: Interstitial Myocarditis Following the Clinical and Experimental Use of Sulfonamide Drugs, Am. J. Path. **18**:109-118, 1942.

2. Maisel, B.; McSwain, B., and Glenn, F.: Lesions Produced with Sulfadiazine, Proc. Soc. Exper. Biol. & Med. **49**:715-717, 1942.

3. Pepper, D. S., and Horack, H. M.: Crystalline Concretions in Renal Tubules Following Sulfathiazole Therapy, Am. J. M. Sc. **199**:674-679, 1940. Stryker, W. A.: The Nature of the Renal Lesions with Sulfapyridine Therapy, J. A. M. A. **114**:953-954 (March 16) 1940. Winsor, T., and Burch, G. E.: Renal Complications Following Sulfathiazole Therapy, ibid. **118**:1346-1353 (April 18) 1942. Lederer, M., and Rosenblatt, P.: Death During Sulfathiazole Therapy, ibid. **119**:8-18 (May 2) 1942. Bradford, H. A., and Shaffer, J. H.: Renal Changes in a Case of Sulfadiazine Anuria, ibid. **119**:316-318 (May 23) 1942. French and Weller.[1l]

Since this paper was submitted for publication an additional case of nephrosis due to sulfonamide compounds has been reported (Sulfonamide Nephrosis, Cabot Case 28501, New England J. Med. **227**:922-927, 1942). Renal phlebitis and multinucleated giant cell changes were striking in this case.

To study the effects of sulfadiazine and of the combination of sulfadiazine and ether anesthesia on the liver, kidney and reticuloendothelial system, the following procedures were employed.

METHOD

Ten mongrel dogs each weighing from 6.2 to 16.4 Kg. were used in the first experiment. Blood was withdrawn for erythrocyte and leukocyte counts, and differential leukocyte and platelet counts were made on blood smears. Determinations of hemoglobin, hematocrit reading, icterus index and prothrombin were made. The urine was examined microscopically; the heat-acid test for the presence of proteins was done, and the acidity or alkalinity was determined with litmus paper.

With the animal under anesthesia induced with sodium pentobarbital, administered intravenously, the abdomen was opened aseptically. Four or five grams of liver was excised, and the abdomen was closed. The glycogen and total carbohydrates in the liver were determined chemically, and sections were stained with Best's carmine stain for glycogen, in addition to routine hematoxylin and eosin stains.

At intervals during the ensuing two weeks, blood was withdrawn for the determinations mentioned previously.

Beginning two weeks after operation, 0.1 Gm. of sodium sulfadiazine per kilogram of body weight was administered twice daily to 6 animals for two weeks. The drug was injected subcutaneously in a 20 per cent aqueous solution. During the two week period blood was frequently withdrawn for the determinations listed, and in addition the levels of the drug in the blood and in the urine were determined. The urine was examined for the presence of protein, blood elements and crystals and for the reaction to litmus paper.

Four weeks after the first operation, under drop ether anesthesia, the 6 treated animals and the 4 controls were again subjected to laparotomy, and a second biopsy specimen was obtained from the liver. The animals were maintained in the surgical plane of anesthesia for three hours, and at the end of this time the studies of the blood and urine were repeated and the animals were killed by injection of ether into the heart. The biopsy specimens from the liver were studied in the manner previously indicated.

At autopsy all organs except the brain, spinal cord, gallbladder, thyroid and parathyroids were examined. Specimens of heart, lung, liver, pancreas, spleen, kidney, urinary bladder, adrenal, thoracic aorta, inferior vena cava, stomach, small intestine, appendix, sternal and costal marrow, skeletal muscle and tissues from the area into which the solution of sodium sulfadiazine had been injected were taken for microscopic examination.

The microscopic observations to be described suggested a study to determine whether the pathologic changes were due to a combination of sodium sulfadiazine, sodium pentobarbital and ether or to sodium sulfadiazine alone.

To a second group of 8 dogs sodium sulfadiazine was administered as it had been to the first group, and treatment was continued up to the time the animal died or was killed. One of the treated animals was killed after eight days and 1 after twenty-one days. Deaths of the remainder occurred at six, nine, ten, twelve, thirteen and eighteen days. The animals which died at six and at ten days had minimal bronchopneumonia that might have been a factor contributory to the cause of death; the deaths of the others were apparently due to sodium sulfadiazine.

The studies in this second group were limited to the determination of the concentration of sulfadiazine in the blood, the urea nitrogen content of the blood and the arterial pressure as measured by femoral puncture. Postmortem examination was done on all animals. In addition to the 4 controls noted previously, 4 apparently normal dogs were killed and used as controls for histologic examination.

RESULTS

1. There were no significant changes in the values for prothrombin, glycogen or total carbohydrate or in the icterus index.

2. A normocytic hyperchromic anemia developed in the 6 treated animals in which the blood picture was studied. No significant changes were noted in the leukocyte, differential cell or platelet counts.

3. The urine of all animals was acid to litmus paper and consistently showed proteinuria and the presence of blood elements, casts and sulfadiazine crystals. In the urine of 6 animals studied on the fourteenth day of treatment, the concentrations of sulfadiazine ranged from 203 to 240 mg. per hundred cubic centimeters.

4. The maximum concentrations of sulfadiazine in the blood were in general high (fig. 1). Ten dogs had maximum levels between 40 and 120 mg. per hundred cubic centimeters. Two dogs had maximum levels of 25, 1 a maximum of 20 and 1 a maximum of 17 mg. per hundred cubic centimeters.

5. In the 8 animals of the second group, there was a marked elevation of the urea nitrogen content of the blood, (fig. 2) the maximum being 111 mg. per

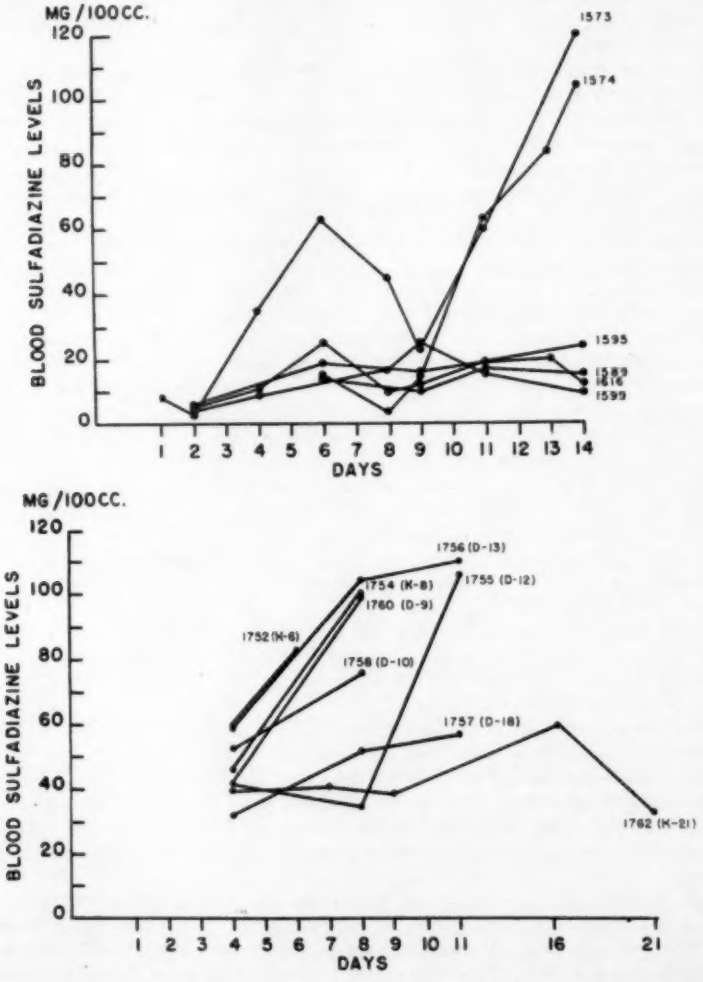

Fig. 1.—Upper chart, concentrations of sulfadiazine in the blood of a group of experimental animals. Lower chart, concentrations of sulfadiazine in the blood of a group of experimental animals. The time of death (*D*) or killing (*K*) is recorded.

hundred cubic centimeters. This elevation tended to follow the level of blood concentration of sulfadiazine (fig. 3).

6. There was a moderate elevation of arterial blood pressure (140 to 160) in 3 animals, a slight elevation (130 to 140) in 2 animals and no elevation (80 to 110) in 2 animals.

7. Grossly, there was sloughing at the sites of injection of the drug in about half the animals. A minimal lobular pneumonia, as previously mentioned, was

found in 2 of the dogs of the second group. There were no gross pathologic changes other than the presence of fine yellow refractile streaking in the pyramids of the kidney, crystals in the renal pelves and calices, and slight swelling of the renal parenchyma of all animals. Chemical analysis of the crystals showed that from 70 to 75 per cent of the material was free sulfadiazine and that the remainder was the combined or acetylated form.

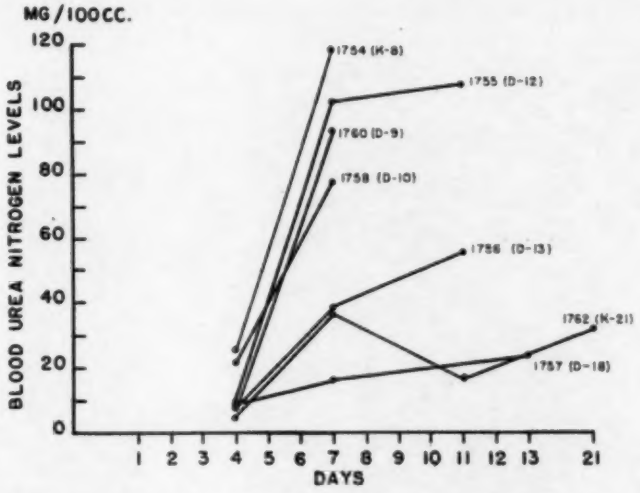

Fig. 2.—Levels of urea nitrogen in the blood. The time of death (*D*) or killing (*K*) is recorded.

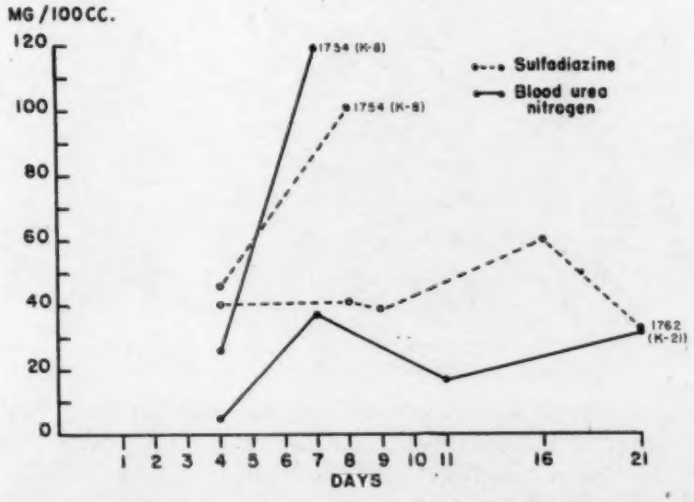

Fig. 3.—There is a rough correlation between a rising level of urea nitrogen in the blood and an elevated level of sulfadiazine.

8. Microscopic pathologic changes were found in the kidneys, spleen, liver, heart and bone marrow and in the tissues removed from the site of injection of the sodium sulfadiazine. These changes were not present in 8 control dogs.

The changes in the kidneys of all animals were most striking. The nephron, the vascular bed and the stroma were simultaneously affected as early as the sixth

day. The characteristics of these changes became more obvious in the animals which received the sodium sulfadiazine for longer periods.

The changes in the glomeruli were first indicated by the escape of blood and protein into Bowman's clear space. Later inflammation developed about the glomeruli, characterized by the presence of monocytes, lymphocytes, plasma cells and a very small number of polymorphonuclear eosinophils and neutrophils. Finally fibroblasts developed and collagen was laid down, forming a granuloma (figs. 4 and 5).

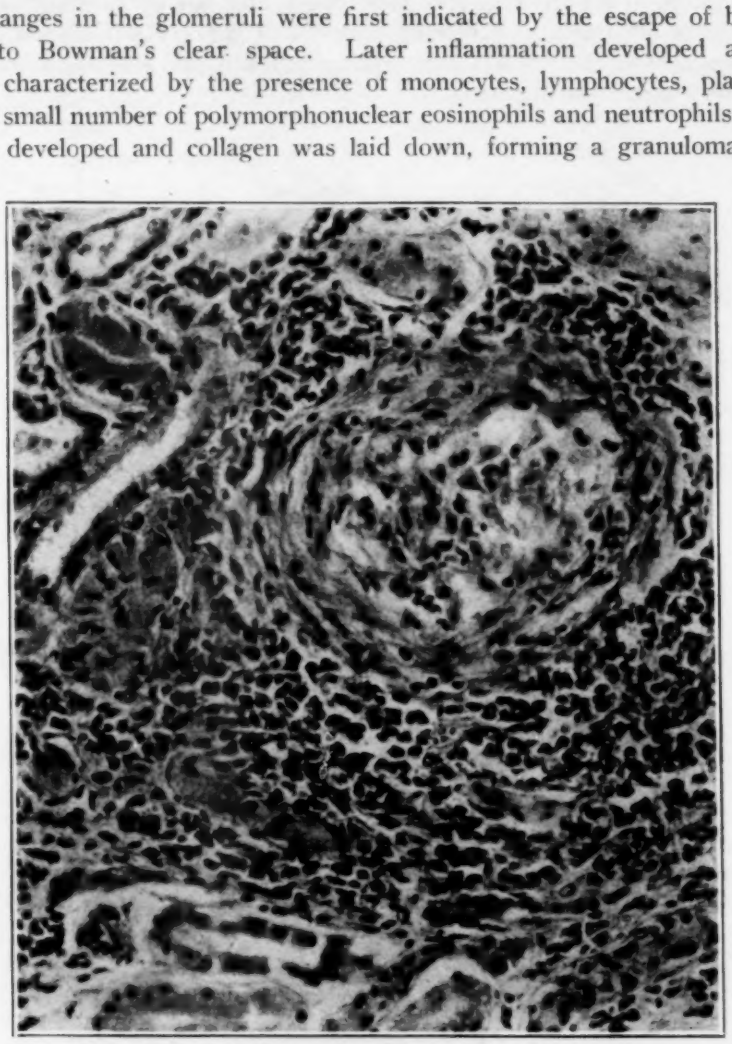

Fig. 4.—Glomerular granuloma showing inflammatory reaction (× 300).

The tubular system of all animals was simultaneously affected, particularly the proximal and distal convoluted tubules and the collecting tubules. The lining cells were swollen, and the cell outlines were not distinct. The nuclei were frequently pyknotic and were often absent. The tubules frequently contained casts of desquamated lining cells. Many of the tubular lining cells were in mitosis. An inflammation similar to that about the glomeruli developed in the stroma about the affected tubules.

The kidney tubules were often filled with a hyaline protein material, metachromatic in its staining qualities. The casts were most often glassy blue and infrequently pink or yellow-brown. In many areas the protein material had escaped into the interstitial tissues through an area of necrosis of the tubular lining cells

and the basement membrane. Inflammation in which monocytes, epithelioid cells, lymphocytes and plasma cells were prominent occurred in these areas. Later fibroblasts grew in and collagen was laid down, and after twenty-one days multinucleated giant cells developed forming a giant cell granuloma (fig. 6).

Crystals of sulfadiazine were found in the cortical and pyramidal tubules of 12 dogs. The crystals were present, many times in a protein cast, as high in the nephron as the descending loop of Henle. The sulfadiazine crystals were found in the calices and pelves of all animals. An inflammatory reaction consisting of cell elements similar to those which developed in the cortical and pyramidal stroma occurred in the submucosal tissues of the calices and pelves of 13 animals (fig. 7).

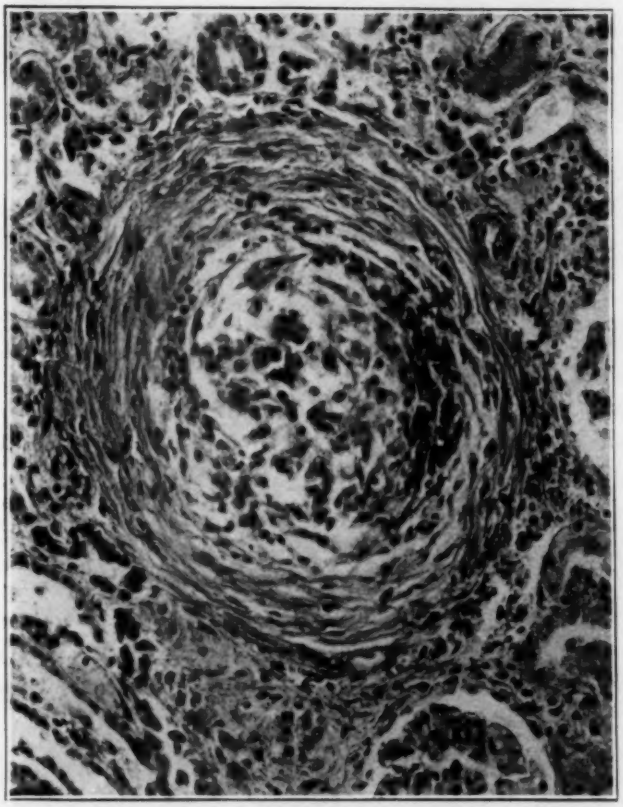

Fig. 5.—Glomerular granuloma showing fibrosis (× 285).

In the walls of and about several of the renal veins of 9 animals, an inflammatory reaction developed which was largely mononuclear in type, with occasional polymorphonuclear eosinophils and neutrophils. Often a mural thrombus was attached to the walls of veins at sites of inflammation. Several small veins were completely thrombosed, and about them fresh hemorrhage was present in the interstitial tissues. A similar sort of inflammation affected the hepatic veins of 3 animals, but no thrombi were noted.

About several of the arteries of the kidneys and occasionally about the arteries of the heart and the liver there was a perivascular leukocyte reaction consisting predominantly of mononuclear leukocytes. Occasionally a few polymorphonuclear eosinophils and neutrophils were present (fig. 8).

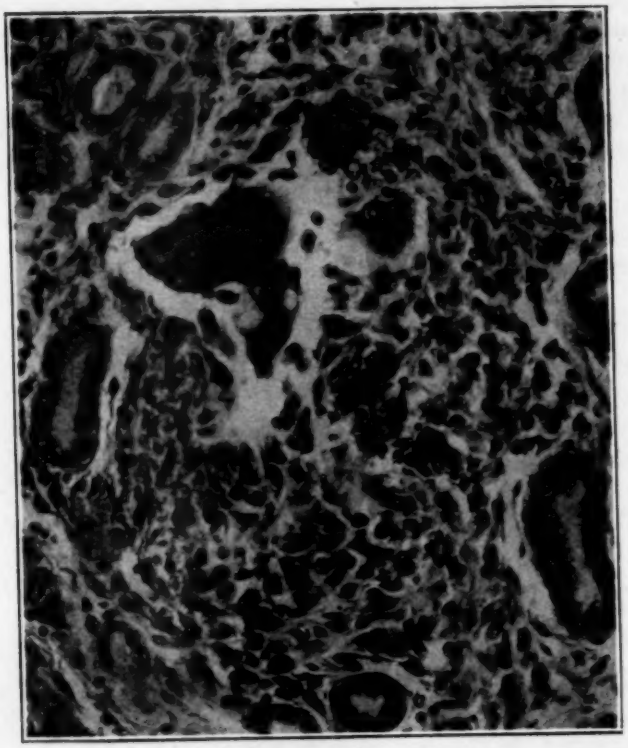

Fig. 6.—Interstitial giant cell granuloma of the renal cortex (× 290).

Fig. 7.—Inflammation in the submucosa of the calix (× 150).

The parenchyma of the liver was normal in appearance in all animals. In 12 animals the Kupffer cells were filled with hemosiderin.

In the spleen all animals had large amounts of both intracellular and extracellular hemosiderin. There was a striking change of the germinal centers characterized by the presence of cellular debris and mononuclear phagocytes, commonly referred to as "toxic" change.

The sternal marrow of 8 animals showed a moderate hyperplasia of all elements, particularly of the erythrogenic series. The marrow of 4 animals contained small areas of recent hemorrhage. In the marrow of 7 dogs there was a moderate amount

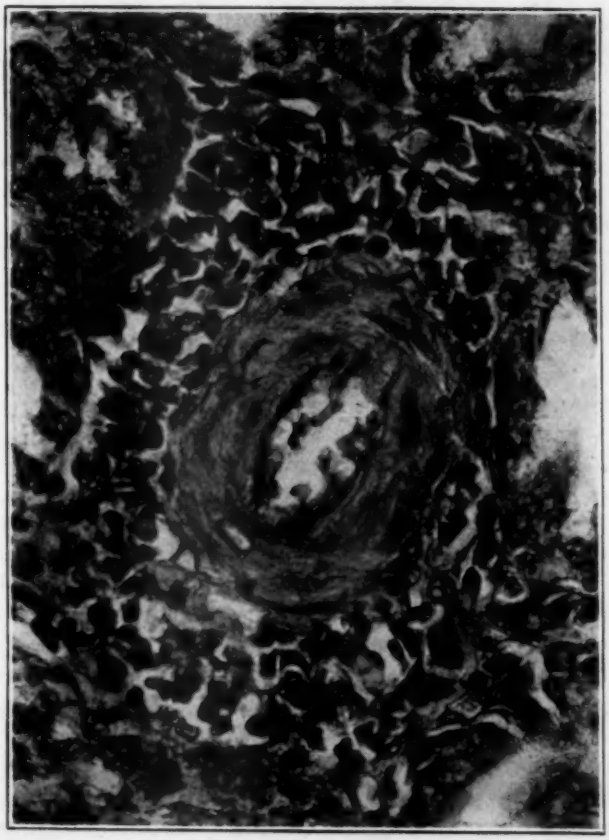

Fig. 8.—Renal artery showing perivascular leukocytic infiltration (× 580).

of hemosiderin in large mononuclear phagocytes. Five animals had either no change or a slight hypoplasia of the marrow. There was a rather marked hypoplasia of the sternal marrow of a single dog. There were small areas of necrosis of the marrow of another animal, and in these areas large mononuclear phagocytes were filled with eosinophilic debris.

Occasional granulomas, consisting of lymphocytes, plasma cells, monocytes, fibroblasts and collagen, were found in the myocardium in 2 animals. The myocardium of 1 dog was the site of small areas of recent hemorrhage.

The tissues taken from the sites of injection of the aqueous solution of sodium sulfadiazine showed almost no loss of tissue-staining quality. Crystals of sulfadiazine were included in multinucleated foreign body giant cells, and there was a

small amount of organizing hemorrhage in these areas. The almost complete absence of polymorphonuclear neutrophil leukocytes from the inflammatory reaction in these areas was striking. The inflammatory reaction was predominantly mononuclear in type, consisting of many monocytes and a moderate number of lymphocytes and plasma cells.

COMMENT

These studies indicate that sodium sulfadiazine injected subcutaneously into dogs produces pathologic changes of the bone marrow, blood, blood vessels and kidneys. The combination of ether anesthesia and sulfadiazine did not alter the changes found following the use of the drug alone.

That renal physiology is disturbed is suggested by the retention of nitrogenous waste products and the elevation of blood pressure in some animals and the development of proteinuria and hematuria in all animals. Hematuria often occurred prior to the development of sulfadiazine crystals in the urine and indicated a primary injury to the renal structures, independent of the effect of tubular obstruction produced by the precipitation of sulfadiazine crystals in the nephron. That sulfadiazine is retained by damaged kidneys is suggested by the high blood levels that developed late in the period of administration.

Sulfadiazine crystals were precipitated not only in the pelvis and collecting tubules but as high in the nephron as the descending loop of Henle. Many subcapsular tubules contained the crystals. Acidity of the urine may be an important factor affecting the precipitation of this drug, and further studies are desirable to ascertain whether the renal damage can be controlled by alkalinization of the urine.

The inflammatory reaction and the granulomas which occurred in the stroma about degenerating tubules and about the pelvis and calices is probably due to irritation by the drug or its product that has escaped into the stroma. These inflammations are characterized by the predominance of mononuclear leukocytes. It is noteworthy that a similar inflammation occurred in the tissues at the site of injection of the aqueous solution of the sodium sulfadiazine. This suggests that both are due to the sulfadiazine or to some changed form of the drug.

The damage to glomeruli and tubules may terminate in the destruction of these structures with formation of a granulomatous lesion, and recovery of a nephron thus scarred seems unlikely. However, most nephrons are not scarred.

Deaths of at least 4 dogs, and probably of 6, of the second group must be attributed to sodium sulfadiazine and were evidently the consequence of damage to the kidneys and the resultant uremia.

The mechanism of the development of hyperchromic anemia is obscure. That erythrocytes are destroyed is indicated by the presence of hemosiderosis in the bone marrow, the spleen and the liver. The hyperplasia of the bone marrow in some animals is probably a response to the destruction of erythrocytes.

SUMMARY AND CONCLUSIONS

Dogs given subcutaneous injections of a 20 per cent aqueous solution of sodium sulfadiazine had initial blood levels of 10 to 15 mg. per hundred cubic centimeters. Within a few days renal insufficiency with rising levels of urea and sulfadiazine in the blood set in, and several of the dogs died in one to three weeks. Some showed a rise in arterial blood pressure; all showed proteinuria and hematuria.

In addition to the deposits of sulfadiazine precipitated in the renal tubules and renal pelvis with granulomatous reactions about them, there were perivascular and even some glomerular granulomas. Instances of phlebitis and interstitial reaction in the kidney and other viscera were more numerous than those reported in other

investigations of the toxicity of sulfonamide compounds. Focal necrosis in bone marrow occurred in 1 of 14 dogs, and hypoplasia of the bone marrow occurred in another. All animals had evidence of hemolytic anemia. Degenerating germinal centers were present in the spleen in nearly all.

Although there was no change in platelets or prothrombin, some visceral petechial hemorrhages were noted. There was no apparent damage to the liver.

The dog, which has an acid urine, shows unusually severe renal damage from doses of sulfadiazine within the therapeutic range. Extrarenal perivascular inflammation is also striking. The relative importance of parenteral deposits of the drug and of the acidity of the urine as factors predisposing to these severe lesions has not been determined.

EPIDERMOID CARCINOMA OF THE ANUS AND THE RECTUM

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Throughout the literature epidermoid, or squamous cell, carcinoma of the anus has been described as a highly malignant tumor offering a poor prognosis regardless of the treatment employed. Such a conception may at present be justifiable in view of the high number of fatalities in all the groups of cases which have been reported. However, the disappointing results responsible for this attitude may be attributed partly to failure of most plans of treatment to take into account the known pathologic aspects of this disease and in a considerable measure to the lack of standardization of treatment. In short, it would seem that in many instances poor results may have been due to inadequate treatment rather than to an inherent incurability of the lesion.

Textbooks and papers dealing with the colon, the rectum and the anus have neglected this anal tumor. In such publications epidermoid carcinoma of the anus is overshadowed almost to the point of exclusion by the vastly more common adenocarcinoma of the rectum. In the occasional papers dealing entirely with squamous cell anal carcinoma, there are few significant statistics relating to mortality based on cases followed five years or longer. Consequently, various methods of treatment which have been advocated are difficult to evaluate, since adequate follow-up data are not available.

In this paper the pathologic and clinical aspects of epidermoid carcinoma of the anus will be summarized. Emphasis will be placed on the considerations governing treatment. Ten cases of squamous cell carcinoma from the records of the Lahey Clinic will be reviewed (table). In 9 of these cases the tumor was anal, while in 1 the growth was located in the rectosigmoid. It is hoped that the various deficiencies in our present knowledge which will become apparent may encourage others to study this disease and report their results.

In approximately 600 cases of malignant rectal or anal neoplasm which have been observed at the Lahey Clinic, squamous cell carcinoma occurred ten times—an incidence of 1.7 per cent. Since figures reported by others [1] vary from 1 to 5.7 per cent, it is safe to say that the incidence is less than 5 per cent of all rectal and anal tumors.

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1. (*a*) Hayden, E. P.: Rectum and Colon, Philadelphia, Lea & Febiger, 1939. (*b*) Buie, L. A., and Brust, J. C. M.: Malignant Anal Lesions of Epithelial Origin, Journal-Lancet **53**:565-571 (Nov.) 1933. (*c*) Raiford, T. S.: Epitheliomata of the Lower Rectum and Anus, Surg., Gynec. & Obst. **57**:21-35 (July) 1933. (*d*) Drueck, C. J.: Types of Anal and Rectal Cancer, Internat. Clin. **1**:196-205 (March) 1927. (*e*) Pack, G. T.: The Pathological Aspects of Anal and Rectal Neoplasia, ibid. **2**:77-90 (June) 1927. (*f*) Hankins, F. D., and Harding, W. G.: Acanthoma of the Anus: Report of Three Cases, Arch. Surg. **29**:77-84 (July) 1934. (*g*) Arons, I.: Radium Therapy and Carcinoma of Anus, Rectum and Sigmoid Colon, Rev. Gastroenterol. **5**:68-79 (March) 1938.

Epidermoid Carcinoma of the Anus and the Rectum: Report of Cases

Case	Age	Sex	Symptoms and Duration	Hinton Reaction	Description of Lesion	Treatment, with Dates	Metastases	Pathologic Report	Follow-Up
1	62	F	Hemorrhoids (3 mo.);	Negative	Ulcerative tumor 4 cm. in	2/25/33, loop colostomy;	None clinically;	Epidermoid carcinoma	Living and well

Case	Age	Sex	Symptoms and Duration	Hinton Reaction	Description of Lesion	Treatment, with Dates	Metastases	Pathologic Report	Follow-Up
1	62	F	Hemorrhoids (3 mo.); rectal pain; constipation; loss of weight, 10 pounds (4.5 Kg.) (5 mo.)	Negative	Ulcerative tumor 4 cm. in diameter, 2 cm. above anal sphincter on right posterior rectal wall	2/25/35, loop colostomy; 3/11/35, posterior resection of rectum	None clinically; laparotomy revealed none	Epidermoid carcinoma, grade 2; lymph nodes normal; tumor extended into muscle but not into perianal tissue	Living and well 4/8/41 (6 years)
2	31	M	Chronic diarrhea up to 20 stools daily (4 yr.); slight bloody mucoid discharge	No report	Induration of perirectal tissues; granulating ulcer on left posterior rectal wall; external hemorrhoid	7/3/30, loop colostomy; 3/11/35, posterior resection of rectum	None clinically; laparotomy revealed none	Epidermoid carcinoma, grade 1	Living and well 1/11/41 (10 years and 5 months)
3	34	F	Hemorrhoids (2 mo.); diarrhea; backache; rectal bleeding; loss of weight, 10 pounds (4.5 Kg.)	.....	Annular hard tumor 1 cm. up and encircling anus completely, invading rectovaginal septum for 5 cm.	9/26/34, palliative loop colostomy; irradiation advised but refused	None; laparotomy revealed none	Epidermoid carcinoma, grade 1	Died at home 3/3/35; no autopsy
4	48	F	Burning sensation in rectum (2 mo.); constipation; diarrhea; loss of weight, 7 pounds (3.2 Kg.) (2 mo.)	Negative	Cauliflower growth; crater-like ulceration 5 cm. in diameter; extended two thirds around rectum on right	9/24/35, first stage Lahey resection, hysterectomy and salpingo-oophorectomy, bilateral; 10/10/35, second stage Lahey resection; 2/27/36, excision of coccyx for recurrence; 4/2/36, subarachnoid injection of alcohol for pain	None clinically; laparotomy revealed none; specimen showed involvement of node 8 cm. up rectum from tumor; 9 nodes normal	Epidermoid carcinoma, grades 1 and 2; uterus, tubes and ovaries normal	Died of local recurrence 5/18/36; no autopsy
5	53	M	Rectal bleeding (2 mo.)	Negative	Large rounded mass extending for 10 cm. up from anus, left posterior aspect of rectum	2/20/37, first stage Lahey resection; 3/11/37, second stage Lahey resection	None clinically; laparotomy revealed none; specimen showed 3 of 7 nodes in perirectal fat involved	Epidermoid carcinoma, grade 1	Postoperative death 3/20/37; no autopsy
6	73	M	Rectal pain; rectal bleeding; rectal prolapse (40 mo.)	Negative	Protruding red beefy tissue on right posterior aspect of anus, arising from mucocutaneous junction	12/2/40, Miles abdominoperineal resection; May 1941, resection of masses in groin	None clinically; laparotomy revealed none; inguinal metastases appeared 5 mo. postoperatively	Epidermoid carcinoma, grades 2 and 3	Living June 1941, with recurrence in inguinal nodes
7	67	F	Vaginal bleeding (4 wk.); perineal pain (3 wk.)	Negative	Ulcerated, granulating, raised tumor 1.5 cm. in diameter involving anterior aspect of anus and adjacent perineum	12/18/39, wide local excision with resection of posterior vaginal wall	None clinically	Epidermoid carcinoma, grade 1	Living and well April 1941, 1 yr. and 6 mo.
8	57	M	Swelling and pain in fistulectomy scar (2 mo.) (excision of fistula 20 years before); purulent anal discharge; slight constipation	Negative	Small, red, round, raised area 1 cm. in diameter; left anal margin; not ulcerated; anal fistula	12/12/39, local excision of tumor and anal fistula	None clinically	Epidermoid carcinoma, grade 1	Living and well 3/16/41 (1 yr. and 4 mo.)
9	63	M	Diarrhea; rectal bleeding	No report	Large cauliflower mass 8 cm. in diameter; anterior aspect of rectosigmoid 10 cm. from anus	2/9/38, first stage Lahey resection; 3/3/38, second stage Lahey resection	None clinically; laparotomy revealed none	Epidermoid carcinoma, grade 3; blood vessel invasion; 5 normal lymph nodes	Living and well 6/2/41 (3 yr. and 4 mo.)
10	71	M	Rectal pain (1 yr.); rectal bleeding (6 wk.); hemorrhoids (6 mo.); loss of weight, 10 pounds (4.5 Kg.) (1 yr.)	Negative	Ulcerated crateriform growth 6 cm. in diameter anterior aspect of rectum adjacent to anus	12/16/40, first stage Lahey resection; 12/20/40, cholecystectomy; 12/26/40, second stage Lahey resection	None clinically; laparotomy revealed none	Epidermoid carcinoma, grade 3; invasion of blood vessels	Living June 1941; tumor had invaded prostate gland and could not be entirely removed

Women are affected more frequently than men. Grouping the statistics of the four largest groups of cases reported,[2] we find the ratio to be 142 women to 107 men. Of the patients in the group on which we are reporting, 4 were women and 6 were men.

The incidence is greatest among those from 50 to 60 years of age. The average age in this series was 55.9 years, with the youngest patient 31 and the oldest 73 years of age. Keyes [2a] reported 57 years as the average age; Raiford,[1c] 48.9 years. All investigators have noted a wide variation in age.

Sufficient data have accumulated to establish antecedent lesions as important causative agents of anal carcinoma. Drueck [1d] went so far as to say that such a tumor always arises on the basis of some previous condition characterized by chronic irritation. Buie and Brust [1b] noted a history of an antecedent lesion in 34 of their 51 cases. As stressed by Rosser [3] and observed by many others,[4] chronic fistulas and scars resulting from fistulectomy are the lesions which have given rise to carcinoma most often. Carcinoma may also arise on the basis of leukoplakia,[3c] a fissure,[3a] hemorrhoids,[2a] venereal condyloma [1f] or an irradiation scar.[2a]

The clinical significance of these causative factors warrants consideration. From a diagnostic viewpoint, carcinoma should be kept in mind in dealing with all rectal and anal lesions, no matter how obviously benign they may appear. A biopsy should be made whenever there is the slightest suspicion of malignancy. Chronicity alone is an ample indication for the microscopic examination of a lesion. All tissue removed during the operative treatment of a supposedly benign lesion should be sent for pathologic diagnosis. This practice is followed at the Mayo Clinic, where it has led to the detection of carcinoma in at least 1 case after microscopic examination of supposed hemorrhoidal tissue.[1b] The pressure of malignant growth was not suspected when the hemorrhoidectomy was performed.

After treatment, operative or conservative, of a benign lesion, it is wise to have the patient report his condition at intervals. If this is not feasible, he should be instructed to seek medical attention promptly if symptoms appear again, for the later episode may possibly be the first evidence of a carcinoma rather than a mere recurrence of the original condition.

Several epidermoid carcinomas arising in irradiated anal skin have been reported.[2a] It is worthy of note that carcinoma has not been reported arising on a basis of uncomplicated pruritus.[3c]

Wassermann tests of the blood gave positive results in 3 cases of anal epithelioma reported by Hankins.[1f] He and several others [3b] have expressed the opinion that syphilis plays a causative role. Whether or not this is true, one should remember that anal cancer may masquerade as syphilis. Wassermann tests of the blood gave negative results in 8 of our cases and were not made in the remaining 2 cases.

One of the 10 patients whose cases we are presenting had a history of a recurrent fistula dating back twenty years. An antecedent lesion was not mentioned by the other 9 patients.

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2. (*a*) Keyes, E. L.: Squamous Cell Carcinoma of the Lower Rectum and Anus, Ann. Surg. **106**:1046-1058 (Dec.) 1937. (*b*) Bensaude, R.; Cain, A.; Oury, P., and Poirier, A.: Le cancer de l'anus, Presse méd. **41**:1837-1842 (Nov. 18) 1933. (*c*) Kerr, J. G.: Squamous Cell Carcinoma of the Anorectal Region, Texas State J. Med. **36**:548-551 (Dec.) 1940. (*d*) Raiford.[1c]

3. Rosser, C.: (*a*) Cancer of the Anal Canal, South. M. J. **28**:527-528 (June) 1935; (*b*) Fistula: An Etiologic Factor in Cancer of the Anal Canal, Texas State J. Med. **30**:203-207 (July) 1934; (*c*) The Etiology of Anal Cancer, Am. J. Surg. **11**:328-333 (Feb.) 1931; (*d*) Relation of Fistula in Ano to Cancer of Anal Canal, Tr. Am. Proct. Soc. **35**:65-71, 1934.

4. Raiford.[1c] Hankins and Harding.[1f] Keyes.[2a]

There is no symptom complex characteristic of anal carcinoma. Rectal pain, occurring chiefly at stool, is the most frequent presenting symptom. Small, repeated rectal hemorrhages are commonly observed. These may take the form of a persistent bloody, mucoid anal discharge. Diarrhea or constipation may be noted, the former more frequently. However, by diarrhea the patient most likely means the frequent passage of small stools or an anal discharge such as has already been described rather than true diarrhea. Itching and irritation around the anus often occur. Less commonly, an anal tumor is the presenting complaint, while in several of the cases reported in the literature [5] enlarged inguinal nodes first attracted the patient's attention.

Six of the patients in our series complained of rectal bleeding, 5 of rectal pain, 4 of diarrhea, 3 of loss of weight, 2 of hemorrhoids, 2 of constipation, 1 of rectal prolapse, 1 of fistula and 1 of anal discharge. These symptoms may occur singly or in any combination. It is obvious that they are no more typical of carcinoma than they are of a number of other rectal diseases.

Fig. 1.—An additional tumor seen in 1941. Epidermoid carcinoma of the anus extending into the right ischiorectal fossa and presenting as an ulcerating cutaneous lesion.

Buie and Brust [1b] reported the average duration of symptoms prior to the time of seeking medical attention as eleven months; Keyes,[2a] as eighteen months. In the 9 cases of this series in which figures were available, the average duration of symptoms was twelve months. However, in 7 of these 9 cases the duration was three months or less.

There is a wide variation in the gross appearance of this type of epidermoid carcinoma (fig. 1). It may simulate a fistula, fissure, chancre, condyloma or hemorrhoid or any other anorectal disease, including, of course, adenocarcinoma. In general the growth tends to be of one of two types: It may be nodular or warty, or it may be flat or craterous. The elevated tumor is often ulcerated; the flat one, nearly always so. Both types are usually of firm consistency, the flat tumor having a hard, granulating base and a firm, rolled edge. It does not seem profitable to enter into further descriptive detail since this aspect of the subject has been so ably dealt with elsewhere. Bensaude and his associates [2b] presented a complete gross description, illustrated by numerous accurate and distinct color reproductions. The papers of Raiford [1c] and Drueck [1d] also contain full descriptions of the gross appearance. Positive diagnosis can be established only by microscopic sections.

5. Keyes.[2a] Bensaude and others.[2b]

Anatomically, the term anus is being used in its broad sense and refers to the perianal and anal skin as well as to the anal canal, which extends upward for a short distance beyond the mucocutaneous junction. Accordingly, anal carcinomas arising from the anal or perianal skin may be located entirely externally, while those arising at the mucocutaneous juncture, a far more common site of origin, tend to extend upward into the anal canal and often into the lower part of the rectum. We feel that the histologic nature of the tumor is more important than its precise location when one is deciding whether or not a growth is anal. A squamous cell tumor in the anal canal or the lower part of the rectum may safely be assumed to have arisen in the anal skin or mucocutaneous junction, though it comes to lie predominately above theses sites. In rare instances a primary epidermoid carcinoma may be found in the colon or the upper part of the rectum. The origin of such a tumor is to be explained only on the basis of cellular metaplasia.[6] An instance of a growth in this location is included in the group of 10 cases which we are presenting, not because we believe that the tumor in this case was related to the anus in any way but because we feel that the rarity of the situation warrants reporting the case.

Epidermoid carcinoma of the anus is similar histologically to epidermoid carcinoma of the skin elsewhere on the body. Some of the growths are well differentiated, being characterized by a uniform type of cell and by epithelial pearls (fig. 2). Conversely, others exhibit a cellular arrangement devoid of order, with a marked variation in the size and shape of individual cells; numerous giant cells and cell nuclei in all states of mitosis may be present (fig. 3). Still other tumors may show histologic types lying anywhere between these extremes of differentiation. Also, the degree of differentiation may vary within the same tumor, as was noted in 2 of our 10 cases (cases 4 and 6). This variation in histologic nature may best be expressed in terms of grading. Kerr,[2c] on the basis of Broders' criteria, found that in the 80 cases of squamous cell carcinoma of his series in which reports were available 4 growths were of grade 1, 17 of grade 2, 41 of grade 3 and 18 of grade 4.

The tumors in the 10 cases which we are reporting were studied and graded microscopically in the laboratory of Dr. Shields Warren. Five of the tumors were found to be of grade 1, 1 of grade 2 and 2 of grade 3. The remaining 2 tumors varied within themselves, 1 showing characteristics of grades 1 and 2 and the other of grades 2 and 3. The possible value of grading in relation to treatment will be referred to later.

Too great emphasis cannot be placed on the importance of the manner of spread of epidermoid carcinoma of the anus, both locally and by metastasis, since this is the basis for treatment. Locally, it may invade the sphincter ani muscles, the perianal tissue, the rectovaginal septum or the prostate gland, or it may extend upward into the rectal wall and rectum.

Metastasis may occur by way of lymphatics or blood vessels. That metastases may be blood borne has been established beyond any doubt. Tumorous invasion of blood vessels (fig. 4) was noted microscopically in the sections from 2 of our cases (cases 9 and 10). Further and conclusive evidence is provided through the fact that metastases to the liver have been observed.[7] These could hardly have occurred by any route except that of the portal venous system. However, metastases to the liver were noted only twice in a group of over 200 cases collected from the literature of the last decade. It is thus apparent that blood-borne metas-

6. Manning, V. R.: Adenocarcinoma of the Anus, Tr. Am. Proct. Soc. **38**:70-74, 1937. Raiford.[1c]

7. Buie and Brust.[1b] Bensaude and others.[2b]

tases are sufficiently uncommon for the possibility of their presence to be disregarded when treatment of the initial lesion is contemplated. In both our cases in which invasion of blood vessels was noted microscopically, abdominoperineal resection was performed, so that abdominal exploration was possible. No evidence of metastatic tumor was noted in the abdomen of either patient. Blood-borne metastases to other organs are rare.

On the other hand, lymphatic metastases are common, and it is the possible or actual presence of these which is most important in the formulation of any

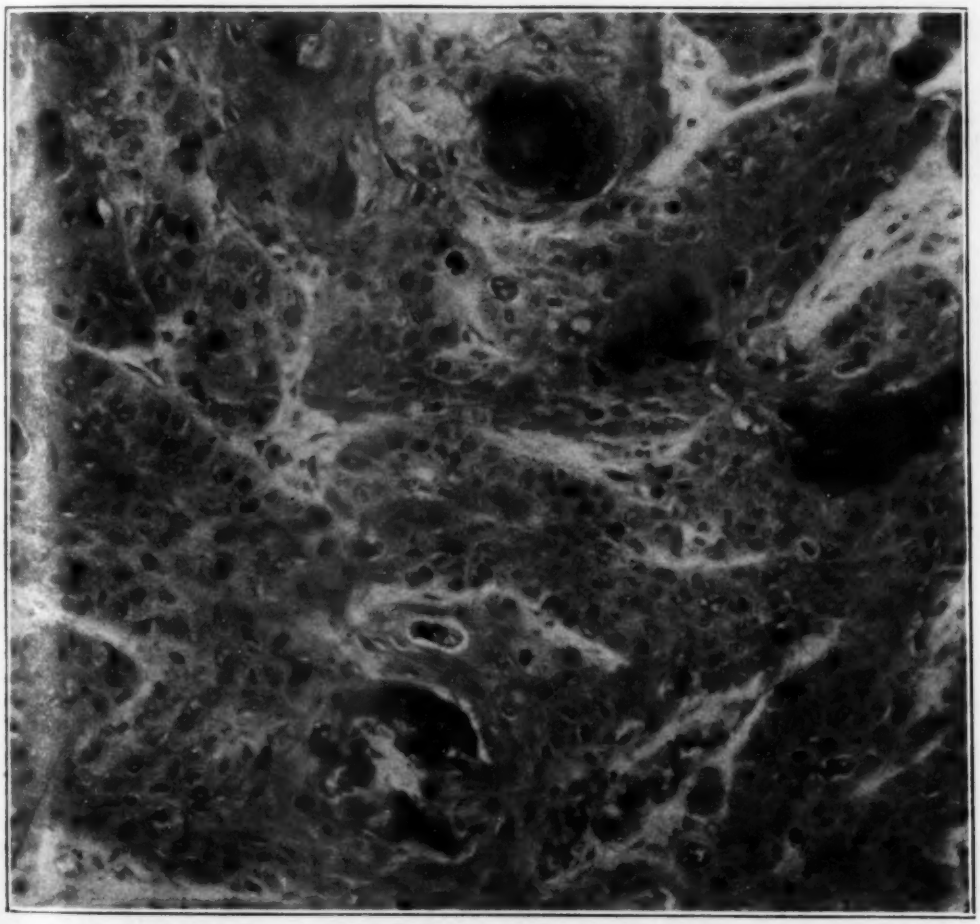

Fig. 2 (case 4).—This tumor is well differentiated. The cells are uniform, but many mitotic figures are noted. Epithelial pearls are present. The tumor was graded 1 and 2 on the basis of this and other sections. The growth had invaded the rectum and metastasized to a node 8 cm. above. The patient died of recurrence in the posterior wound four months after abdominoperineal resection.

plan of treatment. The lymphatic routes of spread of epidermoid carcinoma of the anus are well known and have recently been described in detail by Keyes.[2a] He stressed the fact that metastases from such a tumor are confined almost without exception to the downward and lateral zones of spread described by Miles [8]

8. Miles, W. E.: The Pathology of the Spread of Cancer of the Rectum and Its Bearing upon the Surgery of the Cancerous Rectum, Surg., Gynec. & Obst. **52**:350-359 (Feb.) 1931.

and to the inguinal lymph nodes. The downward zone of spread of Miles consists of the perianal skin, the sphincter ani muscle and the ischiorectal fat. Keyes found this zone to be the one most often involved by metastasis. The lateral zone of spread refers to the levator ani and coccygeal muscles, the pelvic peritoneum, the prostate gland, the base of the urinary bladder, the cervix uteri and the base of the broad ligament. Keyes noted that this zone was involved almost as frequently as the downward zone. He further noted that in his cases the upward zone of spread of Miles, including the rectorectal nodes, the pelvic mesocolon, the para-

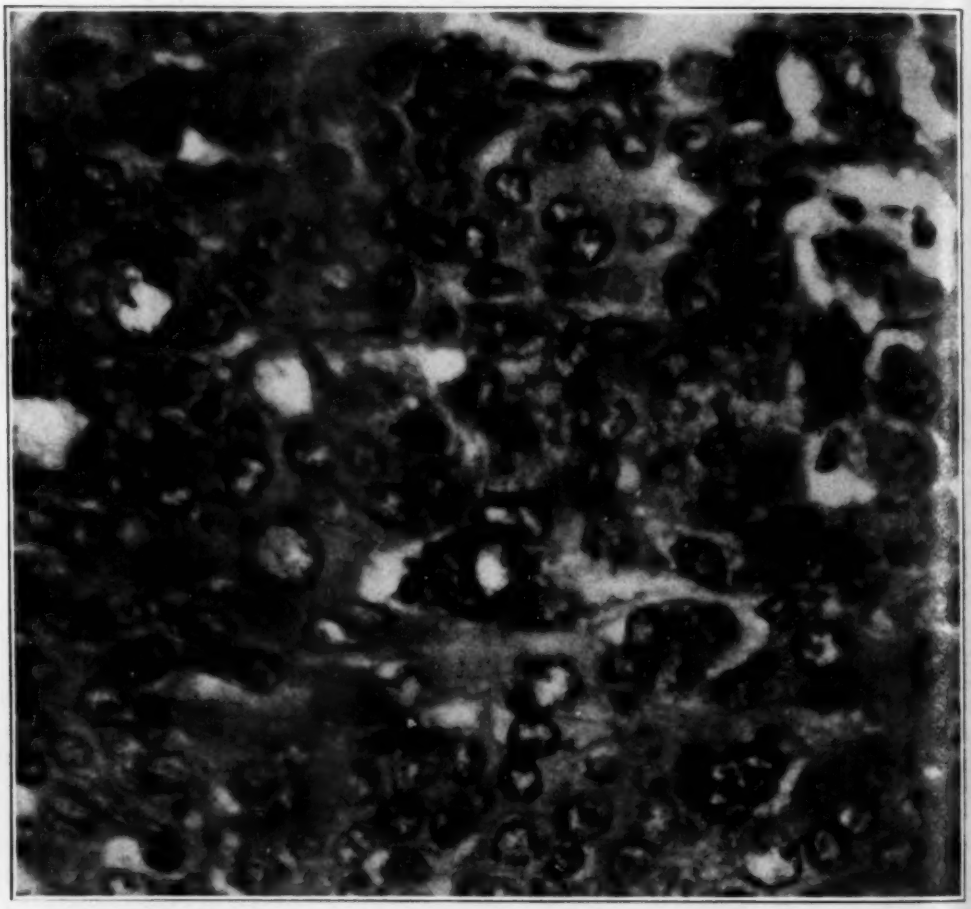

Fig. 3 (case 9).—This tumor was located in the rectosigmoid. Considerable variation in the size, shape and appearance of the cells is seen. Tumor giant cells are present, and cells in various stages of mitosis are plentiful. Another section of this tumor showed invasion of blood vessels. The patient is living and well three years and four months following an abdominoperineal resection. The tumor was classed as grade 3.

colic nodes, the nodes about the bifurcation of the left common iliac artery and the aortic nodes, showed no involvement.

The presence of metastatic carcinoma involving the inguinal nodes was noted in 4 of the 27 cases reported by Keyes. Inguinal metastases are to be anticipated, since the anal skin up to the mucocutaneous junction is drained by lymphatics which lead to the innermost group of inguinal nodes. Lymphatics from the anus pass forward on each side in the fold between the thigh and the perineum to reach

the inguinal nodes of that side.[9] This site of possible metastasis should always be kept in mind and the inguinal nodes examined in every case of carcinoma of the anus. The exact location of a tumor has much to do with the path its metastases take. Tumors below the mucocutaneous junction metastasize to the inguinal nodes most frequently, while tumors above the junction much less commonly involve these nodes but seem to prefer the perirectal tissues.

The only figures of significance relating to the incidence of metastases are those of Keyes.[2a] Metastases occurred in 19, or 70 per cent, of his 27 cases. The impor-

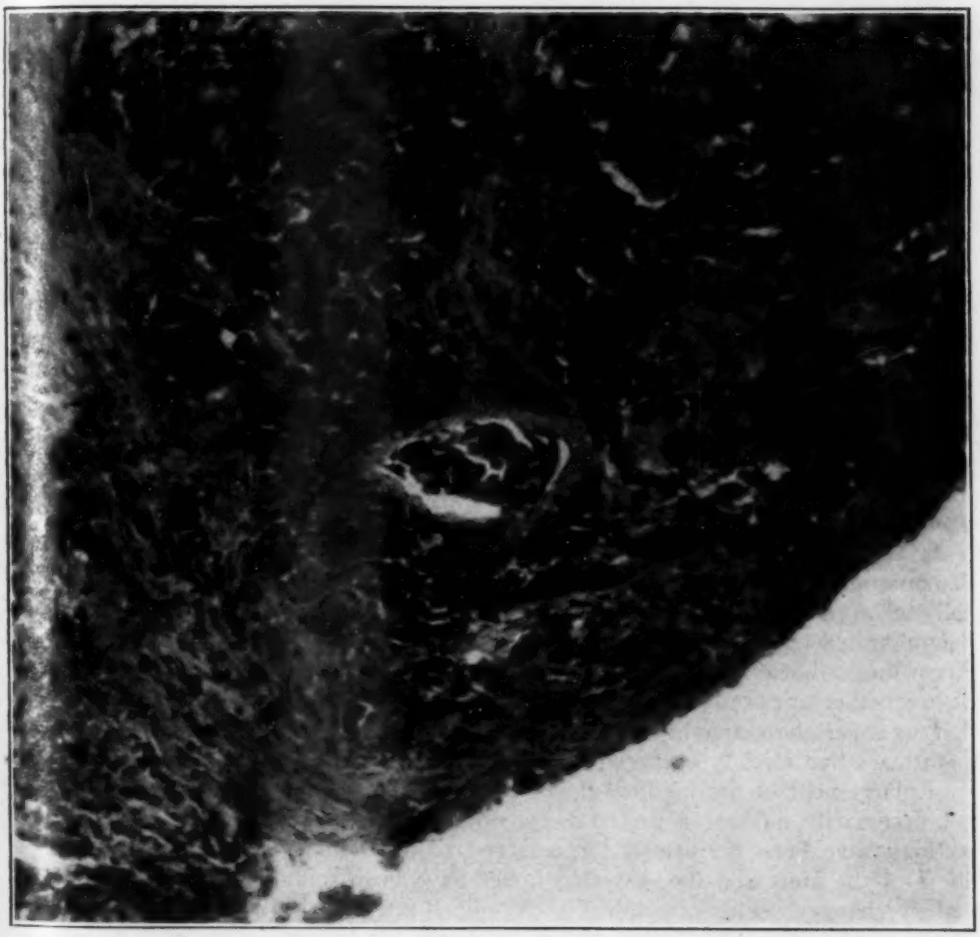

Fig. 4 (case 10).—In the center of the section, tumor cells can be clearly seen in a blood vessel. On the basis of this and other sections the tumor was classed as grade 3. An abdominoperineal resection was performed, but the tumor had invaded the prostate gland and could not be entirely eradicated. The patient has survived six months and has shown no evidence of recurrence up to date.

tance of these figures cannot be too strongly emphasized. This high occurrence rate of epidermoid metastasis makes it obligatory for the physician to regard every patient with epidermoid carcinoma of the anus as having metastases in one or more

9. Nesselrod, J. P.: Demonstration of Genito-Ano-Rectal Lymphatics, Tr. Am. Proct. Soc. **36**:85-90, 1935.

of the regions listed, no matter what may be his conclusions regarding the primary tumor. We feel certain that the failure to recognize these possibilities and the consequent failure to provide for them in the plan of treatment have figured prominently among the causes of poor end results.

Many investigators [10] have pointed out that metastases from squamous cell carcinoma of the anus do not involve the upward zone of spread of Miles. Keyes found that the highest metastasis in his series was located less than 14 cm. above the anus and that this was from a lesion which extended 8 cm. up into the rectum. In 1 of our 10 cases (case 4) a metastatic tumor was noted involving a lymph node 8 cm. above the anus. The primary lesion in this case extended up into the rectum. These sites of metastasis are much higher than usual and, for practical purposes, may be assumed to represent the extremes of upward extension. Anatomically, the upper extreme may be considered to lie somewhat above the level of the pelvic peritoneal reflection off the rectum. This has an important bearing on surgical treatment and will be referred to again in that connection. The nodes most frequently involved are those in the ischiorectal tissues immediately surrounding the anal canal.

These opinions and observations relating to metastases are in agreement with those expressed by most writers on this subject. There is some difference of opinion as to whether metastases occur early or late. In 1 of the cases of our series, inguinal metastases appeared five months after rectal resection. On the other hand, in 2 of the cases reported by Keyes,[2a] inguinal metastases were noted four years after surgical removal of the primary tumor. Fischel [11] noted inguinal metastasis in 2 of his cases after rectal resection. These metastases appeared two years and four years respectively after surgical treatment. There is no way of determining when the inguinal implantation actually occurred in these cases, but it is probable that they were present for some time before they became noticeable. This viewpoint is supported by the studies of Coller [12] and his associates, who demonstrated the presence of metastatic carcinoma in nodes which were not clinically enlarged and which in many instances were so small that they could be demonstrated only through treatment of the tissues by a special clearing process. According, clinical estimates as to when metastases are most likely to occur and as to whether or not they have occurred are no better than guesses. It follows, then, that to cover the common eventualities one must deal with every case as though metastases had already occurred, whether or not they are present clinically.

Enlargement of the inguinal nodes may be on an inflammatory basis and does not necessarily indicate a metastatic tumor. In several instances,[3d] inguinal dissections have been performed for enlarged inguinal nodes associated with carcinoma of the anus and the dissected nodes have been found to show only inflammatory changes. This possibility is mentioned only for its interest and of course should not be allowed to influence one's decision for or against inguinal dissection.

Metastatic involvement of the inguinal glands may occur in patients with adenocarcinoma of the rectum or colon. We have observed this in 2 patients with cancer of the rectum, in 1 with cancer of the rectosigmoid and in a fourth with cancer of the hepatic flexure of the colon. Both of the patients with rectal cancer had extensive involvement of the regional lymph nodes in the zone of upward spread, which suggests that the lateral and downward spread was the result of blocked lymphatics above. The malignant extension in the other 2 patients was

10. Raiford,[1e] Keyes.[2a]

11. Fischel, E.: Cancer of the Rectum, J. Missouri M. A. **33**:419-423 (Nov.) 1936.

12. Coller, F. A.; Kay, E. B., and MacIntyre, R. S.: Regional Lymphatic Metastasis of Carcinoma of the Rectum, Surgery **8**:294-311 (Aug.) 1940.

by means of the peritoneum, since gravity metastases were found in the lower part of the abdomen extending into the inguinal canal and to the inguinal lymph nodes. Three of these patients are dead, and the fourth is living, twenty-eight months after a Miles resection, with intraperitoneal and inguinal metastases.

Of the 10 cases of epidermoid carcinoma which we are reporting, metastases were demonstrable in 2 through the pathologic examination of tissue removed at operation. In 1 of these 2 instances (case 4) there were 9 normal lymph nodes and 1 containing tumor tissue, the tumor-laden node being located 8 cm. above the anus. The primary tumor here was situated in the anal canal and the lowest portion of the rectum. A Lahey two stage abdominoperineal resection was performed, but the tumor recurred in the posterior wound and was eventually fatal. In the other case (case 5) 3 of 7 lymph nodes showed metastasis, these nodes being situated in the perirectal fatty tissue. The patient died eight days after operation. Autopsy was not permitted in either of these cases. In the first of these 2 cases the tumor contained areas classed as grade 1 and other areas classed as grade 2. In the second case the tumor was classed as grade 1. Both the tumors were large and appeared to be growths of fairly long standing.

Involvement of inguinal nodes was not observed in any of our 10 cases when the patients were first examined at the Lahey Clinic. However, 1 of the patients (case 6), on whom a Miles abdominoperineal resection was performed five months ago, has just returned to the clinic complaining of masses in both groins. After excision one of these masses was found to be carcinomatous, while the other showed only inflammatory changes. In this case the primary tumor, showing characteristics of both grade 2 and grade 3, originated at the mucocutaneous junction and was protruding from the anus at the time of the patient's first examination. It did not extend up into the rectum. To date in none of the remaining cases has there been evidence of inguinal metastases, but it is a distinct possibility that such metastases may yet make their appearance.

Abdominal exploration was performed in 8 of the 10 cases and failed to reveal abdominal metastases in any instance.

In the most recent of our cases (case 10) the tumor was found to have invaded the prostatic capsule so that complete removal was impossible. No final statistics can be given as regards metastases, since in only 2 of our 10 cases has five years or more elapsed since the date of treatment.

Treatment.—Epidermoid carcinoma of the anus is fairly radiosensitive, as is the same type of tumor when it occurs elsewhere in the body. Some writers [13a] have advocated therapy by irradiation alone as offering the best chance of cure. Usually radium in some form has been preferred for the control of the primary lesion and inguinal nodes. Interstitial radium applied as radon needles appears to be very effective in producing regression of the primary tumor. Radium element may be administered to the primary growth by means of a perineal applicator or a proctostat. The inguinal nodes have been most frequently treated with roentgen rays, but radium applicators and radon seed have been used as well. Most workers have administered roentgen therapy to the pelvis in addition to the aforementioned measures.

Dosages and methods have varied so with individual investigators that we shall not attempt to present further details. For a description of specific dosages

13. (*a*) Bacon, H. E.: The Present Status of Radiation Therapy in Carcinoma of the Anus, Rectum and Sigmoid Colon, Am. J. Digest. Dis. & Nutrition **3**:255-257 (June) 1936. (*b*) Footnote 7.

and technics, the reader is referred to the paper by Bacon,[13a] in which the methods used by several of the better known investigators are presented.

The immediate response to radiation treatment may be noted in many cases, and cure may be obtained in some cases by this means alone.

Bensaude and his associates [2b] have reported the results in 20 patients treated with interstitially inserted radon needles plus radium administered by a perineal applicator. No details of the treatment of individual patients is given. Of the 20 patients, 1 was free of disease after ten years, 3 after five years, 2 after two years, 1 after one and one-half years and 1 after one year following treatment. In other words, 8 patients were free of disease but only 4 of these, or 16 per cent of the whole group, had been followed as long as five years. On the other hand, in 8 patients tumor recurred at the original site or in the nearby lymph nodes. In the remaining 4 patients the primary lesions failed to regress under irradiation treatment. Therefore, although statistics are incomplete so far as regards five year survivals, it is fairly certain that at least 12 of the 20, or 60 per cent of the patients, were doomed, either through recurrence of disease or through failure of response of the lesion to initial treatment.

The failure of epidermoid carcinoma of the anus to respond to irradiation in some instances has been noted by others.[5] In 11 of the cases of Buie and Brust,[1b] irradiation was the only method employed for destruction of the tumor. In 5 of the patients metastases had developed; 5 were free of disease, and 1 was being treated palliatively. None of them had been followed five years.

In the cases reported in the literature the greatest proportion of the patients who have been subjected to irradiation have been followed for from a few months up to about four years. We can draw no final conclusions from these cases, since it has been repeatedly observed that fatal metastases may not make their appearance until the third to the fifth year following treatment. However, negative conclusions can be reached, for in almost half of the cases in which irradiation was used recurrences had taken place within the first year or two following treatment. Keyes [2a] has noted that inguinal metastases are not amenable to cure by irradiation or by surgical operation, once they are clinically present.

The discomfort incident to irradiation is severe in most cases.

From these considerations we must conclude that present methods of radiotherapy result in eradication of tumor in appreciably less than 50 per cent of the cases. This evaluation may have to be revised pending the appearance in the literature of more complete reports.

Some have favored complete reliance on surgical removal, except in the event of inoperable lesions or inoperable recurrences. Those holding this opinion have favored some form of rectal resection plus dissection of the inguinal lymph nodes. The type of rectal resection advised has ranged from the abdominoperineal operation of Miles to a posterior excision with the formation of a perineal colostomy opening.

Keyes noted recurrences in 11 of his 27 cases, surgical methods having been employed. These recurrent growths appeared either in the posterior wound site or in the groin. The only exception was in 1 case with questionable metastases to the lungs. Six patients of the group were free of disease when last examined. The follow-up period varied from about one and a half to three and a half years. Three of these 6 patients had inguinal dissections in addition to the treatment directed at the primary lesion itself. These inguinal dissections were of a prophylactic nature. It will be extremely interesting to note what happens to these patients. No conclusions can be drawn as yet. Keyes did not mention what types of procedures were employed in the cases in which recurrences developed.

Four of the patients in a series of 43 reported on by Buie and Brust [1b] were alive after five years. In 1 case local destruction of the lesion with cautery was carried out and a colostomy was done; in another local excision plus roentgen therapy was used and in the remaining 2 posterior excision of the rectum was done. Of the 43 patients, 14 were treated by operation alone. Nine of the 14 were free of disease from five months to seven years. Three patients died, and 2 were not followed.

All of the 10 patients comprising the Lahey Clinic group were treated by operation alone. One patient is living and well ten years and another six years after treatment, both having had colostomy and posterior rectal resection. Three patients died. One of these (case 3) had had a loop colostomy and refused further treatment of any sort. There was 1 postoperative death (case 5) after a second stage Lahey resection. The third death (case 4) was due to recurrence in the wound. A two stage Lahey resection had been done in this instance. Recurrence in the site of the posterior wound led to resection of the coccyx, but a second recurrence was fatal.

One patient (case 6), already referred to, is in the hospital now with incurable inguinal metastases which appeared five months after a Miles abdominoperineal resection was performed.

The remaining 4 patients are well to date, having survived free of disease for from six months to three years and four months. To summarize our present results, 6 patients are well after from six months to ten years and a seventh is living with extensive metastases to the groin.

It is obvious that these surgical results do not lend themselves to final evaluation. However, several important conclusions are evident. In general, the operative procedures performed in the past and at present are not extensive enough to eradicate all tumor tissue in the average case. Such an operation as excision of the lesion with the cautery or posterior excision of the rectum will yield cures in the earliest, most favorable cases but when applied to average cases will push the number of recurrences up to a formidable figure. We may further conclude that metastases when clinically present cannot be eradicated by a surgical operation. Important is the fact that almost all observers to date have remarked on the rarity of intra-abdominal metastases. Abdominal exploration was performed in 8 of our 10 cases, and gave negative results in every instance. Summarizing results to date, operation alone has been more effective than irradiation alone. These results point toward radical operation as the type of therapy offering the best prognosis.

Therapeutic combinations of irradiation and surgical intervention have been widely employed. Raiford [1c] suggested external irradiation followed by radical surgical intervention. Hayden [1a] advised surgical resection of the rectum followed by roentgen therapy to the inguinal lymph nodes. The possible combinations are numerous, as is shown by the variation in the treatment administered in the cases reported by Buie and Brust.[1b] This multiplicity of methods makes any attempt at evaluation worthless. Buie and Brust [1b] concluded that either surgical treatment or irradiation is satisfactory if applied with sufficient aggressiveness.

Hankins [1f] suggested that surgical treatment is best in dealing with tumors of grades 1 and 2 but that irradiation is more effective against grades 3 and 4. Kerr [2e] has clearly shown what we would naturally expect, namely, that the mortality rate is much higher with tumors of grades 3 and 4 than with those of grades 1 and 2. The former tumors metastasize earlier and more widely. However, metastases are common with tumors of lower grade malignancy; hence one has no right to employ a more conservative type of surgical treatment for tumors of these grades. Nor does it seem reasonable to abandon operation in favor of irradiation for tumors of grades 3 and 4 because their malignancy is greater and their mortality higher. Few of

these can be cured by irradiation, while a considerable number are amenable to radical surgical treatment. We believe that grading of anal carcinoma is valuable in formulating a prognosis. But when one uses it as a guide to determine the method of therapy to be employed one is attempting to draw lines where no definite lines can be drawn. We believe radical surgical treatment offers the patient the best chance of cure, regardless of the histologic gradation of his tumor, and we believe that all patients with operable lesions are entitled to this type of treatment.

In attempting to formulate such a plan of surgical treatment it is necessary first to define the potential extent of the pathologic process to be eradicated. The primary tumor must be dealt with, including the surrounding tissues which may be involved by direct extension. These tissues include the anal skin and a wide area of perianal skin, the anal sphincter, the rectum, the ischiorectal fat, the levator ani muscles and usually the posterior wall of the vagina. Possible sites of lymphatic metastases must be taken into account. These include the lymph nodes in the ischiorectal fat and the levator ani muscles, the rectorectal nodes, the mesocolic nodes and any nodes lying under the peritoneum of the pelvic floor. Also, one must include the nodes of both inguinal regions and the iliac glands.

Removal of the tissues just enumerated will require two operative procedures, an abdominoperineal resection and a bilateral inguinal dissection. The method of abdominoperineal resection described by Miles is adequate for the treatment of the lesion itself and the regional metastases which may be present. Any one of several other methods are also adequate, provided they are as radical as the procedure of Miles. A permanent abdominal colostomy opening should be made in all cases. The inguinal dissection should include both the femoral, inguinal and iliac nodes along with the surrounding fatty tissue. No effort is made to remove the lymphatic vessels leading from the anus to the groin.

Both these procedures should be performed in every case of an operable tumor in which cure is possible and feasible. Deviations from this approach should be limited strictly to cases in which the lesion is obviously beyond cure and the only goal is palliative relief. We have no hesitancy in performing inguinal dissection when the glands are known to be involved for the relief of pain or to avoid ulceration.

The inguinal dissection should follow the abdominoperineal operation, with at least seven days intervening. The dissection will be a prophylactic procedure in most instances but is nevertheless essential in every case. Enlarged inguinal nodes are no contraindication to the dissection, since the nodes may be inflammatory and it is only through such a dissection that the presence or absence of metastases to the groin can be established.

Contraindications to operation are few. A tumor is considered inoperable only if it has obviously invaded some structure, such as the prostate or broad ligaments, from which it cannot be resected. Rarely will a patient be found who is too poor an operative risk to be subjected to a surgical procedure.

We feel that irradiation should be reserved for patients who, for one of the foregoing reasons, cannot be operated on and for patients having a nonresectable recurrent tumor. In cases of operable cancer irradiation may be used as an adjunct to but not as a substitute for radical operation. We have had no experience with preoperative or postoperative irradiation.

COMMENT

As has been brought out, the foregoing discussion deals only with squamous cell, or epidermoid, carcinoma. The clinical distinctions between this type of anal tumor and other types, such as basal cell carcinoma and adenocarcinoma, are not as

great as the histologic differences would imply. All these tumors show a tendency to metastasize to the lymph nodes in the groin as well as to the nodes about the anus and the lower part of the rectum. Adenocarcinoma, as Keyes pointed out, differs from epidermoid carcinoma in that it fairly often spreads to the lymph nodes of the sigmoid mesocolon and to the liver. Basal cell carcinoma, on the other hand, remains localized as a rule and has a much lower incidence of metastases than does squamous cell carcinoma. Instances of metastases to the groin from an anal basal cell tumor have been reported, however.

We are watching with particular interest the patient whose lesion was located in the rectosigmoid (case 9). This patient is free of disease, having had a two stage Lahey resection of the rectum three years and four months ago. The tumor was histologically of grade 3 and showed invasion of the blood vessels.

Neither surgical treatment nor irradiation has been radical enough in the past. End results following both types of therapy would no doubt be much improved if radical methods were instituted and standardized. We feel that five year survival rates should rise from 60 per cent to 80 per cent with the acceptance of radical operation as the method of choice in every case. The procedure suggested is the minimum which will give satisfactory results in the greatest number of cases. The rectal resection should include resection of the coccyx, posterior vaginal wall or other resectable tissues which happen to show involvement. Especial pains should be taken to excise a wide area of perianal skin, as was advocated by Miles. It is hoped that the practice of local excision for so-called favorable lesions will be abandoned. These favorable lesions will give most favorable results if treated radically, whereas one is courting recurrence and a fatality in over 50 per cent of the cases if one employs local excision alone.

Prophylactic inguinal dissection was proposed and carried out by Keyes. We feel that the idea is sound, especially since the outlook is hopeless once the nodes in the groin are clinically involved. Final opinion of this procedure must wait.

The operative mortality over the past three years in cases of all types of lesions of the rectosigmoid, rectum and anus in which the Miles abdominoperineal resection has been used at the Lahey Clinic has been 7 per cent. No mortality statistics are available for radical inguinal dissections in patients having epidermoid carcinoma of the anus. The combined operative mortality rates of these two procedures should not exceed 10 per cent. One death in our group of 10 cases was an operative death.

SUMMARY AND CONCLUSIONS

Treatment of epidermoid carcinoma of the anal region has been attended by poor results in the past, regardless of the method employed.

Ten cases of epidermoid carcinoma have been presented. In 9 of these the growth was anal, while in 1 the tumor occurred in the rectosigmoid.

Microscopic study of all anal and rectal lesions is urged, in order that carcinoma may never be overlooked when present.

Various methods of therapy have been reviewed. It is our conclusion that radical operation offers the best prognosis. A surgical approach consisting of a Miles abdominoperineal resection and a radical inguinal dissection is advocated for every operable growth. This recommendation is based on a detailed pathologic and clinical study. Irradiation is indicated for inoperable lesions and for recurrences following operation.

DERMOID AND EPIDERMOID TUMORS (CHOLESTEATOMAS) OF THE CENTRAL NERVOUS SYSTEM

REPORT OF TWENTY-THREE CASES

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Publications appearing from time to time since Verattus [1] first described a dermoid variety of tumor in 1745 have told so well the story of neoplasms of this type that it has become familiar to those interested in the subject. Because of confusion in nomenclature and controversies regarding pathology, it seems essential to reconsider some of the earlier works in this field. We trust that it may crystallize concepts concerning these unusual neoplasms.

Most articles dealing with the history of dermoids and epidermoids have referred to the excellent review by Bostroem [2] in 1897. According to Mahoney [3] the first communication regarding an epidermoid came from Pinson,[4] an artist in the School of Medicine of Paris, in the year 1807. He prepared a wax model of such a tumor located in the region of the cerebellum and fourth ventricle and described its grayish white interior and silvery white capsule. Dupuytren included the model in the school collection, and Chazel made a beautiful reproduction of it for Cruveilhier's Atlas. Several authors, including Horrax [5] and Critchley and Ferguson,[6] stated that Duméril [7] demonstrated this model and reported the case before the Société de Médecine. According to Critchley and Ferguson, Cruveilhier, referring to this case twenty years later, stated it had occurred in Dupuytren's service at the Hôtel-Dieu about 1803-1804.

Epidermoids were next described by Rudolphi [8] in 1813, by Parent-Duchatelet and Martinet [9] in 1821, and by Le Prestre [10] in 1828. The following year, in his famous "Anatomie Pathologique," Cruveilhier [11] fully described the tumor of Pinson and Duméril, which, because of its highly refractile and nodular surface, he termed *tumeur perlée*. At the same time he reported a parapituitary epidermoid

1. Verattus, M. V.: De Bononiensi scientiarum et artium instituto atque academia commentarii, Bononiae, 1745, vol. 2, pt. 1, p. 184.

2. Bostroem, E.: Ueber die pialen Epidermoide, Dermoide und Lipome und duralen Dermoide, Centralbl. f. allg. Path. u. path. Anat. **8**:1, 1897.

3. Mahoney, W.: Die Epidermoide des Zentralnervensystems, Ztschr. f. d. ges. Neurol. u. Psychiat. **155**:416, 1936.

4. Pinson: Bull. École de méd. de Paris **2**:32, 1807; cited by Mahoney.[3]

5. Horrax, G.: A Consideration of the Dermal Versus the Epidermal Cholesteatomas Having Their Attachment in the Cerebral Envelopes, Arch. Neurol. & Psychiat. **8**:265 (Sept.) 1922.

6. Critchley, M., and Ferguson, F. R.: The Cerebrospinal Epidermoids (Cholesteatomata), Brain **51**:334, 1928.

7. Duméril, A. M. C.: Bull. Fac. de méd. de Paris **1**:32, 1807; cited by Mahoney.[3]

8. Rudolphi, K. A.: Arch. f. med. Erfahrung **1**:508, 1813.

9. Parent-Duchatelet, A. J. B., and Martinet, L. M.: Recherches sur l'inflammation de l'arachnoïde cérébrale et spinale, Paris, Crevot, 1821, p. 439.

10. Le Prestre, F.: Tumeur adipociriforme dévelopée dans le mésocéphale, Arch. gén. de méd. **18**:5, 1828.

11. Cruveilhier, J.: Anatomie pathologique du corps humain, Paris, J. B. Baillière, 1829, vol. 1, book 2, plate 6 and p. 341.

in an 18 year old girl. He was the first to describe completely the origin and pathologic character of these tumors. In 1834 Peyrot [12] reported an epidermoid just posterior to the pons and adherent to the cerebellum, which he believed to be identical in character with that already described by Cruveilhier.

In 1838 Johannes Müller,[13] noting the association of cholesterol crystals with these tumors, introduced the name "cholesteatoma." He gave a complete gross and microscopic description of 3 such neoplasms, one of which was the first diploic epidermoid to be described. Virchow,[14] studying 4 cases in 1854, suggested a return to the name of pearly tumor. He felt "cholesteatoma" was a misnomer because cholesterol was neither an essential nor a constant finding in these tumors.

Esmarch [15] in 1856 and Bailey [16] in 1920 gave a brief account of what appears to have been the first surgical treatment of an epidermoid, namely, a diploic tumor of the frontal bone.

Eventually it was felt that "pearly tumor" described only a limited class of cholesteatomas, merely implying that some tumors of this general group had a pearly luster because of the highly refractile quality of their covering. The non-hair-containing epidermoid variety revealed this peculiarity most strikingly, the pearly sheen depending on whether only the upper, and not the lower, or dermal, layer was included in the tissue of origin. Bostroem [2] and Horrax [5] have, however, reported cases in which the cholesteatoma gave the characteristic appearance of pearly tumor and yet contained hair, showing that this highly refractile covering was not confined to the non-hair-containing variety. Such findings emphasize the almost certain general relationship of these tumors. As Kato [17] has pointed out, the occasional reports of certain intracranial teratomas show that the deeper layers may be involved or the cell inclusions may have further potentiality.

Bostroem [2] in 1897 described them as "pial epidermoids and dermoids, and dural dermoids," because he felt their supporting tissue was thus best represented. His opinion, however, remains controversial, and the term most frequently associated with this variety of tumor continues to be "cholesteatoma." Horrax [5] modified this to "meningeal cholesteatoma," believing this eliminated the group of tumors containing cholesterol crystals which arise from pituitary rests. Such a term eliminated confusion with the cholesteatomas of the middle ear, which do not have primary meningeal attachment.

Critchley and Ferguson [6] expressed the opinion that "epidermoid" was more suitable than other terms employed, since it was brief and accurate and conveyed the idea of the epithelial nature of the growth. They emphasized the fact that "epidermoid" could be readily used in contrast to "dermoid" tumors of analogous origin but containing elements other than mere epidermal structure. In 1937 Munro and Wegner [18] divided the tumors into "primary cranial and intracranial epidermoids and dermoids," believing that the concept was thus made more exact. From recent publications it is becoming increasingly evident that the terms "dermoid" and "epidermoid" are most frequently used in describing these neoplasms.

12. Peyrot, M.: Tremblement mercuriel. Sudamina. Tumeur comprimant le cervelet, Arch. gén. de méd. **4**:620, 1834.

13. Müller, J.: Ueber den feineren Bau und die Formen der krankhaften Geschwülste, Berlin, G. Reimer, 1838, vol. 1, p. 50.

14. Virchow, R.: Ueber Perlgeschwülste, Virchows Arch. f. path. Anat. **8**:371, 1854.

15. Esmarch, F.: Cholesteatom in Stirnbein, Virchows Arch. f. path. Anat. **10**:307, 1856.

16. Bailey, P.: Cruveilhier's "Tumeurs Perlées," Surg., Gynec. & Obst. **31**:390, 1920.

17. Kato, T.: Ein kasuistischer, Beitrag zur Kenntnis von teratoiden Geschwülsten in Kleinbrückenwinkel, Jahrb. f. Psychiat. u. Neurol. **35**:43, 1914.

18. Munro, D., and Wegner, W.: Primary Cranial and Intracranial Epidermoids and Dermoids, New England J. Med. **216**:273, 1937.

INCIDENCE

According to earlier statistics, Tooth [19] found but 1 cholesteatoma in a series of 258 cerebral tumors, and Bernhardt [20] 1 in 487. The dermoid variety has been described less frequently than the epidermoid. In 1922 Horrax,[5] adding 3 more to those already reported in the literature, brought the total number of cases to 26. Bailey,[16] on the other hand, had accounted for 62 epidermoids in 1920, making that type of cholesteatoma appear about twice as common. Horrax [5] observed, however, that of 750 verified intracranial tumors in the Brigham series, 3 tumors each of the dermoid and of the epidermoid variety occurred, either type thus representing 0.4 per cent of all intracranial growths.

In 1936 Love and Kernohan [21] expressed the opinion that fewer than 100 epidermoids had been described at operation or necropsy. In the same year Mahoney,[3] on the other hand, in an extensive review of the literature, was able to collect 142 cases. Since then numerous individual reports have appeared. In 1937 Munro and Wegner [18] described a diploic epidermoid, an intracranial dermoid and an intracranial epidermoid. In 1938 Askenasy [22] reported 5 intracranial epidermoids and 1 spinal epidermoid. In 1939 Alpers [23] added 1 diploic epidermoid and 7 intracranial epidermoids. Later in the same year King [24] reported 1 intraspinal epidermoid, 3 intracranial epidermoids and 4 diploic epidermoids. In contrast to this number of epidermoids, Brock and Klenke,[25] in a review published in 1931, were able to collect only 39 cases of intracranial dermoids. Kornfeld [26] in 1930 brought this number to 48, and Courville and Kimball [27] in 1936, to 56.

The series here reported includes 23 cases, 11 of which are instances of diploic, or cranial, epidermoid. Two of the cases, both of dermoid, were reported previously by one of us (C. W. R.). The first was a case of intracranial dermoid cyst of the left temporal region reported in 1925, and the second an instance of dermoid cyst of the inferior cerebellar vermis reported in 1936. Our series represents cases of tumors of this type observed in patients admitted to the neurosurgical service or discovered on postmortem examination at the Los Angeles County General Hospital, as well as cases of such neoplasms studied in private practice. At present, as far as we know, fewer than 200 epidermoids of the central nervous system have been reported.

REPORT OF CASES

A. DIPLOIC OR CRANIAL EPIDERMOIDS

CASE 1.—*Diploic epidermoid of the right frontal region previously operated on as a sebaceous cyst; complete removal and recovery.*

19. Tooth, H. T.: The Treatment of Tumours of the Brain, and the Indications for Operation, Tr. Internat. Cong. Med., London (sect. 11, Neuropath.), 1913, p. 252.

20. Bernhardt, M.: Beiträge zur Symptomatologie und Diagnostik der Hirngeschwülste, Berlin, A. Hirschwald, 1881.

21. Love, J. G., and Kernohan, J. W.: Dermoid and Epidermoid Tumors (Cholesteatomas) of the Central Nervous System, J. A. M. A. **107**:1876 (Dec. 5) 1936.

22. Askenasy, H.: Les tumeurs perlées du névraxe, Encéphale **1**:209, 1938.

23. Alpers, B. J.: Cerebral Epidermoids (Cholesteatomas), Am. J. Surg. **43**:55, 1939.

24. King, J. E. J.: Extradural Diploic and Intradural Epidermoid Tumors (Cholesteatoma), Ann. Surg. **109**:649, 1939.

25. Brock, S., and Klenke, D. A.: A Case of Dermoid Overlying the Cerebellar Vermis: A Review of the Literature on Intracranial Dermoids, Bull. Neurol. Inst. New York **1**:328, 1931.

26. Kornfeld, M.: Ueber intrakranielle dysontogenetische geschwülstartig Bildung an der Hand eines pialen, sekundär stark veränderten Dermoids am Kleinhirn, Virchows Arch. f. path. Anat. **278**:165, 1930.

27. Courville, C. B., and Kimball, T. S.: Subpial Dermoid Cyst of Inferior Cerebellar Vermis, Bull. Los Angeles Neurol. Soc. **1**:84, 1936.

In 1926 a 13 year old boy first noticed a small swelling in the right frontal region, which gradually increased in size until it became about as large as a walnut. In September 1929 he was operated on for a supposed sebaceous cyst of the scalp. At this time, however, it was discovered that the cyst extended through the inner table of the skull. A considerable amount of cheesy material was removed, and the wound was closed without drainage. After healing by first intention the cyst subsequently refilled, and the wound broke down, discharging a thin, brownish fluid which contained the same sebaceous material.

During the months following the patient complained of gradually increasing headache, unassociated with nausea or vomiting. On Feb. 6, 1930 he accidentally struck his head and immediately complained of a severe headache and vomited. That evening his temperature rose to 104.5 F. The following morning he complained of severe headache and pain in the back of the neck and vomited frequently.

Examination.—The patient was vomiting and irrational. His neck was stiff, and the Kernig and Babinski signs were present bilaterally. It was believed the patient had an epidermoid cyst in the right frontal region, which, having become infected, ruptured when he struck his head the day previous. Roentgenograms of the skull showed a round, smooth, punched-out area which appeared old. On subsequent examination the characteristics of a diploic epidermoid (fig. 1) were noted. Lumbar puncture yielded a cloudy fluid containing 4,140 cells.

Fig. 1 (case 1).—Roentgenogram of right lateral view of the skull showing the defect in the right frontal region characteristic of a diploic epidermoid.

The globulin content was considerably increased. A Gram stain revealed numerous polymorphonuclear leukocytes and rarely gram-positive cocci in pairs. There was leukocytosis, the white cell count being 60,700.

Operation on February 8 revealed a grayish, soft mass of tissue resembling cerebral cortex. On tapping, a small amount of brownish fluid containing plaques of caseous-appearing tissue escaped. A cyst 2 cm. in diameter was then removed, along with part of the bone about the osseous defect. No cerebral abscess was present. The patient made an uneventful recovery and left the hospital on February 25. On Jan. 20, 1937 he reported that he was in good health and had had no further trouble.

Unfortunately no pathologic report was obtained, but from the roentgenograms and the gross appearance at operation the diagnosis of diploic epidermoid seemed certain.

CASE 2.—*Dermoid cyst in the midline anterior to the anterior fontanel; complete removal and recovery.*

A 5 month old boy was referred because of a small swelling in the midline of the skull anterior to the anterior fontanel. This was noticed shortly after birth. Polydactylism was also present, there being an extra toe on each foot and the remnant of an extra finger on each hand.

Examination.—The baby, a well developed boy, weighed 16 pounds (7.3 Kg.). Just in front of the anterior fontanel and directly in the midline was a small swelling, symmetric and domelike, measuring 2 by 2 cm. in diameter and elevated approximately 1 cm. above the surrounding scalp. It was somewhat fluctuant and slightly movable but showed no evidence of inflammation. Roentgenograms of the skull showed a defect in the midline anterior to the anterior fontanel and underlying a soft tissue tumor (fig. 2).

On Jan. 27, 1932, a tumor measuring approximately 2 by 2 cm. was easily dissected out. It was oval, well encapsulated and bound to the top of the longitudinal sinus by fine adhesions. It was not lobulated. The patient's postoperative course was uneventful, and he was discharged from the hospital February 6.

Microscopic sections through the center of the cyst showed the cavity to be filled with a structureless debris. Squamous epithelium lined the cavity, and some keratin existed on the surface of the epithelium. The dermal layer was present, but true papillae of the papillary layer were not seen because of flattening from distention by the contents of the cyst. The reticular layer was present, showing both superficial sebaceous glands and deeper sweat glands with numerous scattered hair follicles. A diagnosis of dermoid cyst was made.

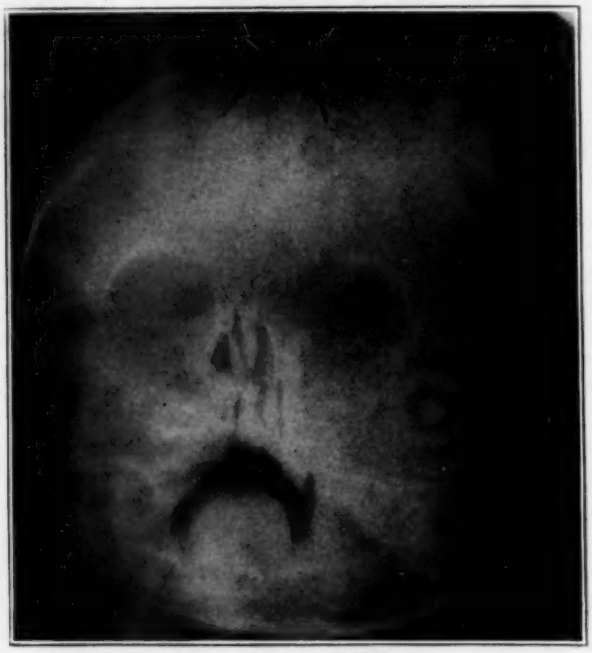

Fig. 2 (case 2).—Cranial defect in the midline anterior to the anterior fontanel at the location of the cranial dermoid.

CASE 3.—*Diploic epidermoid to the left of the external occipital protuberance eroding through the outer table of the skull; complete removal and recovery.*

A single woman of 23 years was admitted to the hospital Feb. 7, 1936, complaining of intermittent headaches and ringing in the ears. About a year prior to this admission she had begun to have lapses of memory, which gradually increased in frequency.

She had been seen by one of us (C. W. R.) five years previously, after an automobile accident, when a small swelling was noted in the occiput. Roentgenograms at that time revealed a peculiar defect in the skull in the region of the external occipital protuberance. A crater-like area measuring about 1.5 cm. in diameter, involving only the external table, was noted. It did not appear to be a fracture, but was believed to be the result of an old pathologic process. An epidermoid, however, was not suspected. The neurologic examination gave negative results, and her symptoms were believed to be due to a cerebral concussion.

Examination.—The patient seemed nervous and emotional. The head showed a soft, slightly cystic, round tumor 2.5 cm. to 3.5 cm. in diameter in the occipital region just to the left of the external occipital protuberance. It seemed attached to the calvarium.

The patient was seen again by one of us (C. W. R.) on February 21, when an oval cystic area in the bone, measuring approximately 4 by 5 cm. in diameter, was found. On palpation a mass about as large as a hen's egg was felt directly over the external occipital protuberance. It had the same peculiar fluctuant quality which had been previously noted. The mass, however, had increased in size. In view of a recent experience with a cholesteatoma in the occipital region (case 6), a similar lesion was suspected. Roentgenograms of the skull

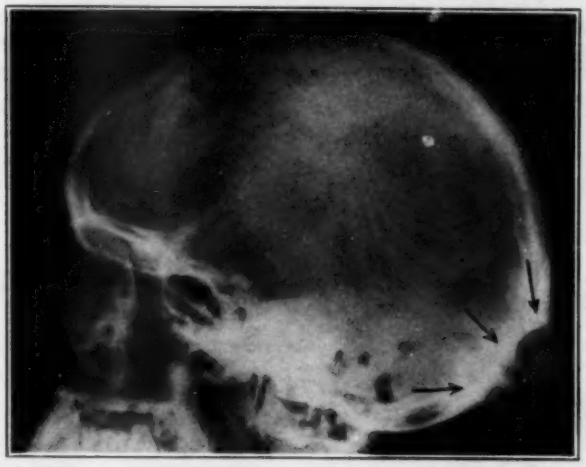

Fig. 3 (case 3).—Lateral roentgenogram of the skull, showing the defect in the occipital region.

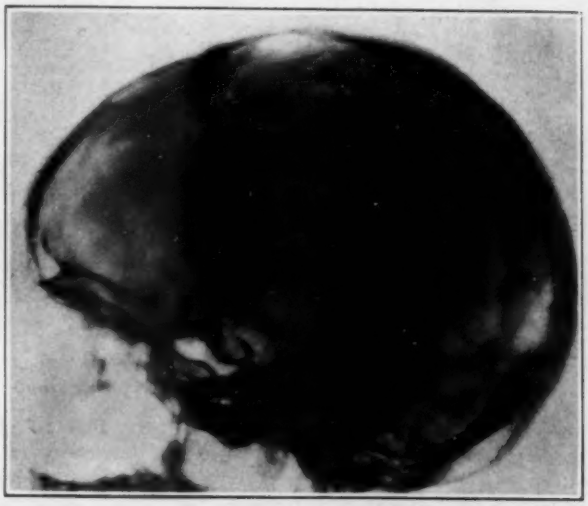

Fig. 4 (case 4).—Lateral roentgenogram, showing the diploic epidermoid in the left parietal bone.

taken February 10 revealed a multilocular cystic lesion of the occipital bone extending left from the midline and associated with swelling of the soft tissue. The Wassermann and the Kahn reaction of the blood were reported negative.

On February 24 Dr. G. H. Patterson removed a large epidermoid that had eroded the outer table in the area of the occipital protuberance. The inner table was thinned but intact. The patient made an uneventful recovery, being discharged on March 5. Pathologic examination, both gross and microscopic, revealed a typical epidermoid.

Comment.—That diploic epidermoids may be confusing unless one has their identifying roentgenographic characteristics in mind is evidenced by the foregoing case. The occurrence of injury to the head five years previously complicated the diagnosis. A review of the earlier roentgenograms showed them to be characteristic of a diploic epidermoid (fig. 3).

CASE 4.—*Diploic epidermoid of the left parietal region; four operations with final complete removal and recovery.*

A girl of 18 years was operated on for a supposed sebaceous cyst of the scalp in the left parietal region by another physician on Oct. 30, 1933. She had been conscious of its presence for five years. During this time it had slowly increased in size. Examination revealed a tumor in the left parietal region about 3 cm. in diameter and 2 cm. above the flush of the scalp. It was movable and did not seem to be attached to the bone.

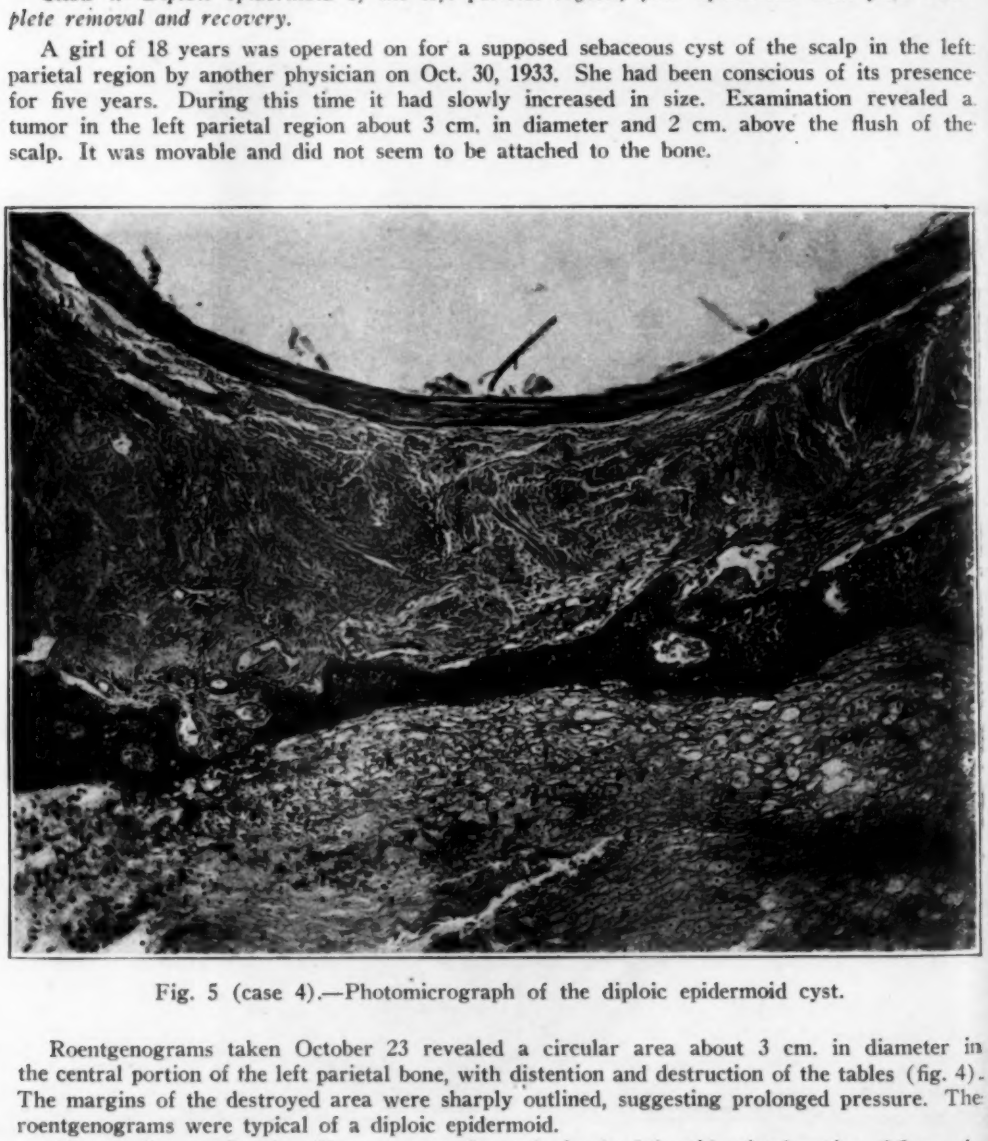

Fig. 5 (case 4).—Photomicrograph of the diploic epidermoid cyst.

Roentgenograms taken October 23 revealed a circular area about 3 cm. in diameter in the central portion of the left parietal bone, with distention and destruction of the tables (fig. 4). The margins of the destroyed area were sharply outlined, suggesting prolonged pressure. The roentgenograms were typical of a diploic epidermoid.

At operation on October 30 a mass on the scalp in the left midparietal region, 2.5 cm. in diameter and extending through the outer table of the skull, was found. It was intimately connected with the inner table. The cyst was filled with sebaceous material. It was removed and the depression in the skull thoroughly cleansed. The specimen after gross examination was reported as containing 1 Gm. of yellow, flaky sebaceous material. A few pieces were covered on the surface with a thin layer of pearly white substance. A thin, membranous strip of tissue having a smooth, gray inner surface was found. This was believed to be a cyst wall. Although the gross appearance of the tumor was that of an epidermoid, it was considered a sebaceous cyst at the time.

Because of recurrence of the tumor, the patient was reoperated on twice in 1936 at two month intervals. At the fourth and last operation on Aug. 19, 1937, the mass was completely

enucleated, the bone curetted and a portion of the scalp immediately above the mass removed. There has been no recurrence. Microscopic sections of the material revealed a typical epidermoid cyst (fig. 5).

CASE 5.—*Diploic epidermoid of the right frontal region eroding through the outer table of the skull. Complete surgical removal and recovery.*

A Negro woman of 44 years was admitted to the hospital in June 1934, complaining of a swelling in the right frontal region of two years' duration. Questioning revealed that she had first noticed a mass in the right supraorbitofrontal region when she was 8 years of age. By 1932 the mass had increased in size, but it was never painful. Her general health had always been good. The Wassermann reaction of the blood was positive.

Examination.—A tumor mass about 6 cm. in diameter was found overlying the right frontal region. It had a soft, cystic consistency at its vertex, but merged with the bony substance below. It was felt that she had a benign cystic tumor of the soft tissues of the right frontal sinus.

Roentgenograms of the skull taken May 29, 1934 were reported as showing large areas of cystic degeneration in the right frontal region which were not distinctive in appearance. Some type of benign tumor mass, not connected with the intracranial structures, was suspected.

Fig. 6 (case 5).—Lateral roentgenogram of the skull, demonstrating the cranial epidermoid in the right frontal region.

At operation, on July 30, the sebaceous material forming the contents of the cyst, but not the wall of the cyst, was removed. Closure was carried out without drainage. At this time it was not suspected that the tumor was an epidermoid, and the pathologic diagnosis was given as cystic tumor, nonmalignant, type undetermined.

The patient was followed in the outpatient department, where the recurring cyst was aspirated frequently. Eventually the patient was examined in the neurosurgical department. The previous roentgenograms were reviewed and were considered to be characteristic of a diploic or cranial epidermoid (fig. 6). On June 29, 1938 Dr. H. G. Crockett completely removed the tumor and its sac. The tumor had eroded the outer table of the skull, causing a defect about the size of a walnut. The inner table was intact. Convalescence was uneventful. The pathologist reported a small cyst containing flaky white material and numerous other fragments of fibrous tissue. Gross and microscopic examination confirmed the diagnosis of epidermoid cyst.

CASE 6.—*Convulsive seizures for seven years; roentgenograms revealing characteristic findings of an epidermoid; operative removal of a diploic epidermoid cyst; recovery.*

A woman of 54 years gave a history of convulsive seizures occurring once or twice a week during the previous seven years. Consciousness was lost for a few minutes, but no jerking of the extremities was observed. A chewing motion of the jaws accompanied some of the attacks, and occasionally her seizures were preceded by a peculiarly dreamy state in which things seemed far away. There was no history of aphasia or headaches.

Examination.—The head revealed no unusual irregularities or tenderness. Except for hypertension (her blood pressure was 215 systolic and 115 diastolic) and a precordial enlargement, the results of general physical examination were essentially negative. The optic disks seemed a little pale, but the remaining neurologic examination showed normal conditions.

Roentgenograms of the skull revealed a discrete shadow measuring about 4.5 by 3.5 cm. in diameter far forward in the right temporal region, which appeared to be in the wall of the temporal and frontal bones. It had the appearance of a diploic epidermoid (fig. 7).

At operation on Sept. 27, 1934 a cyst lying between the inner table of the skull and the dura in the right temporal region was exposed. Its wall was thin, bluish and for the most part friable. Greenish fluid was first liberated, followed by grayish, cheesy, grumous material. Except for its atypical color, it resembled the contents of an epidermoid. The cyst occupied the recess between the temporal and the frontal lobe and dipped down deeply into the sylvian fissure. The bony opening was enlarged to permit removal of the outer wall of the cyst. Except for the portion close to the zygoma, an attempt to dissect the sac from the dura was unsuccessful. The remaining tags of the wall of the cyst were treated with Zenker's solution. The patient made an uneventful recovery.

Dr. R. W. Hammack reported that the specimen consisted of a considerable amount of yellowish, sometimes slightly greenish, soft, structureless material in which there were numerous glistening fine crystals. Some small pieces of tissue represented the lining of the

Fig. 7 (case 6).—Lateral roentgenogram, revealing the diploic epidermoid in the right temporal region.

cavity. Microscopic examination of the soft material revealed numerous cholesterol crystals, but no identifiable epithelial cells. Sections of the tissue consisted of hyaline and necrotic fibrous connective tissue in which were numerous spaces surrounded by cells of inflammatory origin and often by foreign body giant cells. Small spaces lined by cuboidal epithelial cells were found. A diagnosis of epidermoid cyst was made.

CASE 7.—*Large diploic epidermoid in the midoccipital region; incomplete removal and recovery.*

A man of 32 years was referred on Feb. 11, 1933. About September 1934 he first noticed a swelling in the occipital region. During December 1934 his eyes tired easily, and there was noticeable blurring of vision. About this time dizziness on sudden change of position appeared. Increasing dizziness was not accompanied by unsteadiness of gait.

Examination.—There was a swelling in the region of the external occipital protuberance, measuring 7 by 6 cm. in diameter and elevated about 2.5 cm. above the surface of the scalp. The swelling consisted of both hard and soft components; the soft area, measuring 3.5 cm. in diameter, was most elevated and showed definite pulsation, which could be seen and felt. No murmur was heard. Bilateral papilledema of about 4 diopters was present, but otherwise the general neurologic examination gave negative results.

Roentgenograms showed a defect in the middle of the occipital bone nearly twice as large as the foramen magnum, the upper margin being practically at the torcula and the lower margin about 1 cm. above the foramen magnum (fig. 8). The lateral view showed some calcification along the outer border. The Wassermann reaction of the blood was negative.

An epidermoid approximately 5 by 7 cm. in diameter was exposed on March 8, 1935. This was filled with grumous material containing large flakes, some resembling pearls. The lining membrane was thin, glistening, pearly and trabeculated. The portion of the membrane which could not be completely removed was treated with Zenker's solution. The osseous defect, measuring about 5 by 6 cm., involved both the inner and the outer table. The patient made an uneventful recovery.

Fig. 8 (case 7).—Posteroanterior view, showing the cranial epidermoid in the occipital region.

Fig. 9 (case 8).—Lateral view, with the epidermoid defect evident in the left frontotemporal region.

Dr. R. W. Hammack reported flat epithelial cells and cholesterol crystals. A diagnosis of epidermoid was made.

CASE 8.—*Diploic epidermoid of the left frontal region; operative removal and recovery.*

A woman of 65 years was first seen on Oct. 6, 1936 and complained of a swelling in the left frontotemporal region which was first noticed after she struck her head against a stove about fourteen years previously. The tumor had increased in size during the last six weeks. Convulsions began at 35 and continued at about monthly intervals until three years ago, when they subsided. Considerable headache followed the attacks, and she at times was

unable to speak, although she knew what she wished to say. This patient was right handed and had never had any difficulty with reading or writing. She had taken phenobarbital regularly for the past three years.

Examination.—A swelling measuring approximately 4 by 5 cm. in diameter and elevated about 1 cm. above the surrounding scalp was noted in the left frontotemporal region. The scalp was freely movable over the underlying mass and did not seem to be affected. The swelling was neither reddened nor tender. No other unusual irregularities were discovered. Roentgenograms of the skull showed an oval defect in the left frontotemporal region, measuring 3 by 3 cm. in diameter (fig. 9), having the appearance of a diploic epidermoid. The Wassermann reaction of the blood was negative.

The patient was operated on on October 15, when the outer table was opened over the tumor and about 15 cm. of black blood was liberated. The remaining contents consisted of what appeared to be broken-down, degenerated tissue. The inner table was eroded through in some places and very thin in others. As much of the tumor tissue as possible was removed as well as the involved bone. An uneventful recovery was made.

She was last seen on Aug. 2, 1939, having had a convulsion about three weeks previously and a second attack a week later. The area of osseous defect in the left temple remained unchanged. A slight pulsation was obtained on coughing. General physical and neurologic

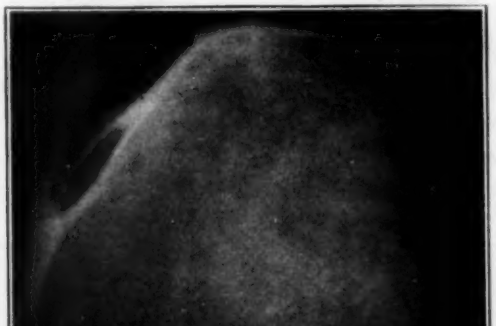

Fig. 10 (case 9).—Posteroanterior roentgenogram, showing separation of the inner and the outer table by the cranial epidermoid.

examinations gave negative results. Review of the roentgenograms showed them to be characteristic of a diploic epidermoid. Microscopic examination revealed bits of striated muscle, fibrous connective tissue and small spicules of bone. Fibrous connective tissue, in which were many large mononuclear cells with a foamy, granular cytoplasm, was found between the spicules of bone. In other areas a fibrous connective tissue was observed in which were many cleftlike spaces from which crystals, probably cholesterol, had been dissolved. About these were some multinuclear giant cells. No epithelial elements were seen in the tissue. There was no evidence of malignancy. Dr. Angus Wright was of the opinion that the histologic picture was that of an epidermoid growing within bone.

CASE 9.—*Gradually enlarging tumor of the left parietal region, first noticed at the age of 9 years; operative treatment at the ages of 34 and 36, and again at the age of 44; continued drainage since that time; further removal of a large infected diploic epidermoid July 1937, at the age of 64; with subsequent recurrence and two additional operations; death from bronchopneumonia in April 1939; autopsy.*

A 64 year old carpenter had first noticed a swelling, which was thought to be a wen, in the left parietal region at the age of 9 years. At 30 he was struck on the head by a piece of timber. At this time the tumor ruptured, but subsequently healed without treatment.

After this it grew more rapidly, and when the patient was 34 it was the size of an orange. At this time he was operated on at Shenandoah, Iowa; the contents of the tumor were emptied but the capsule was not entirely removed. After a short period of drainage the wound closed. The tumor again increased in size and was reoperated on two years later. Again the wound drained for a short time before closing. After remaining quiescent for a few years, it increased in size slowly. No information was available concerning pathologic observations made in these two procedures.

On Feb. 2, 1917, at the age of 44, he was examined at the Mayo Clinic. He was operated on there, for the third time, on March 10, 1917, by Dr. J. C. Masson, who removed a large quantity of foul, broken-down, sebaceous material. A large cavity, measuring 3 by 2 (7.5 by 5 cm.) inches in diameter, extending through the outer table of the skull in the parietal region was noted. No pathologic report is available. After operation the wound continued to drain. Later the odor from the drainage became offensive. The discharge consisted of a cheesy material together with foul greenish fluid. The wound required frequent dressings, as many as three or four a day in the later years of the patient's life.

About April 1, 1937 inflammation developed over the left side of the scalp. This increased rapidly and was painful. A cellulitis developed involving the entire left side of the head. As the swelling subsided, a residual area of fluctuation high up in the parietal region was noted. An area of bone destruction measuring approximately 10 by 8 cm. in diameter was seen in the roentgenograms at this time. The outer table was principally affected, but in one area the inner table appeared to have been eroded through. At one point in the anteroposterior view separation of the inner and outer tables was seen (fig. 10).

Examination.—The entire left side of the scalp was boggy. In the midparietal region was an old sinus tract. A fairly definite osseous defect, measuring approximately 10 by 8 cm. in diameter, could be felt in the skull. Rather high toward the left frontal region there was an area of fluctuation under the scalp. The area of fluctuation was drained April 23, 1937. On July 22, when the left parietal region was reexplored, an abundance of infected granulation tissue was uncovered. The inner table of the skull had been eroded over an area 5 by 5 cm. in diameter. Above this erosion was a mass of pearly white avascular tissue, such as is usually seen in the contents of a cholesteatoma. Surrounding this material was a definite thick sac, apparently lined by epithelium. Above this was an area of osteomyelitis of the skull. The entire mass was dissected out, and the diseased bone was removed by rongeurs. The dura was not ruptured. Anteriorly the cyst had grown between the inner and outer tables of the skull and was separating them. The case was believed to be that of a typical large diploic epidermoid. The history was unusual in that three operations had been performed without complete removal of the tumor.

Dr. A. G. Foord reported epidermoid cyst with extensive chronic inflammatory change. No conclusive evidence of malignancy was discovered, although some portions of the microscopic sections were suggestive.

When the patient was seen Aug. 26, 1937 there was a small discharging sinus with a characteristic odor. It was believed there might be a small area of infected bone beneath. When he was again examined, September 22, the wound was still discharging. Some flaky tissue suggestive of an epidermoid cyst was liberated. It was thought advisable to reexplore the wound. This was done September 24. In several places remnants of the epidermoid cyst were found, and newly forming, cheesy, whitish debris was encountered. The osteomyelitis had advanced toward the midline of the skull. The infected bone and as much of the remaining epidermoid as possible were removed. Suspicious areas were coagulated with the electrocautery, as was the under surface of the scalp. Although it had been believed that all remnants of the sac were removed by the first procedure, this was disproved by the second operation. It was hoped that no subsequent reformation of the cyst would occur, but on this occasion the operator was dubious such would be the case. Dr. A. G. Foord reported epidermoid epithelium with profound hyperkeratosis.

After the second procedure, aphasia and weakness of the right hand developed, which were believed secondary to cauterization of the dura. These symptoms improved steadily, so that on October 14 the patient was able to use the right hand well, although not so well as the left, and at the same time his speech was much improved. He still experienced difficulty in reading. When he was again seen, Jan. 25, 1938, swelling and inflammation of the upper frontal region were present and recurrence of the epidermoid was thought to be evident. Another exploratory operation was performed February 1. The recurrent epitheliomatous growth was removed and all remnants of the growth on the dura cauterized thoroughly. The wound was again closed with drainage. His condition remained essentially unchanged until the latter part of April 1939, when pneumonia developed. He died April 23. Autopsy revealed the immediate cause of death as bronchopneumonia. Sections through the

ulcerative area of the parietal region disclosed tongues of fairly well differentiated cells which seemed to be invading the tissue (fig. 11). The pathologic findings were considered to be fairly suggestive of squamous cell carcinoma.

CASE 10.—*Diploic dumbbell type of epidermoid in the right parietal region; operative removal and recovery.*

A 21 year old college student, while playing football on Nov. 27, 1937, was kicked on the right side of the head. He was not rendered unconscious. Toward night he began having severe headache accompanied by attacks of vomiting. The following day the headache continued to be very severe. Stiffness and soreness of the neck developed. He was taken to a hospital, where blood-tinged fluid was obtained on spinal puncture. He left the hospital December 1, feeling much better. Further questioning revealed that during the previous six months he had noticed a firm swelling in the right parietal region near the injured area.

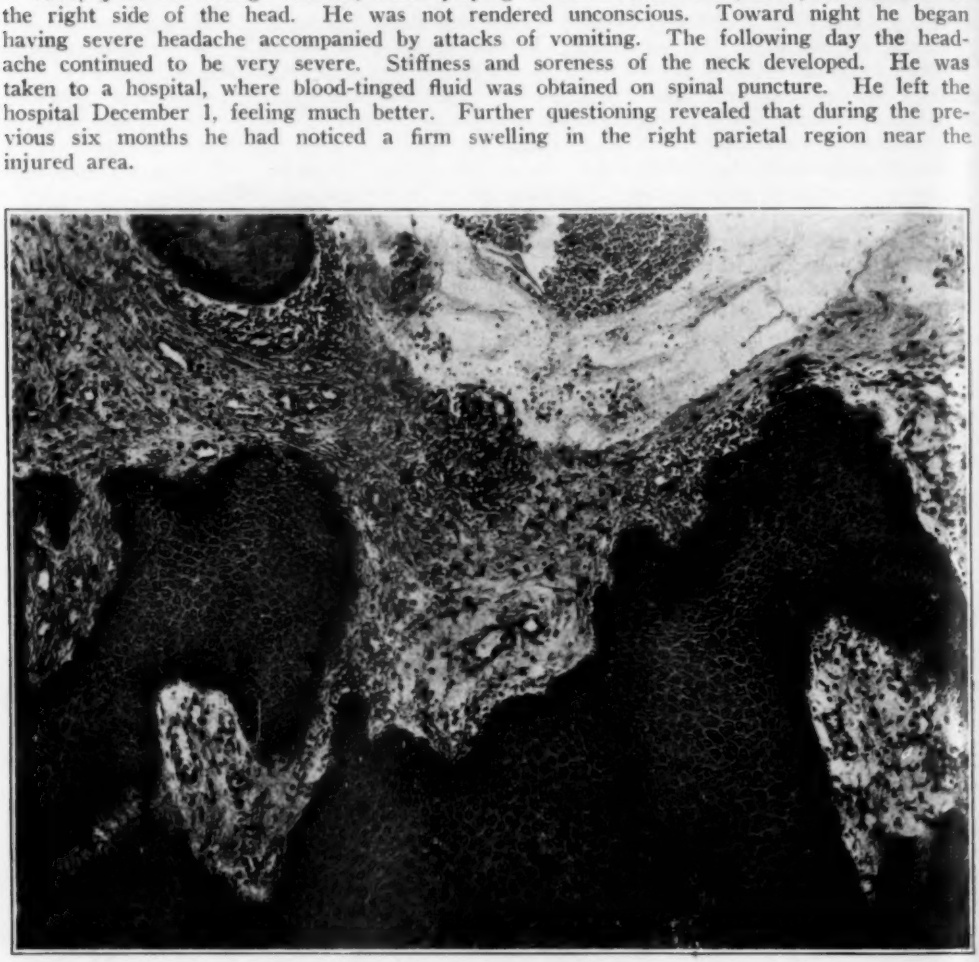

Fig. 11 (case 9).—Photomicrograph of the epidermoid, revealing extensive hyperkeratosis suggestive of squamous cell carcinoma.

Examination.—There was slight stiffness of the neck, and he complained of some headache and backache. In the right parietal region one could feel a depression in the skull admitting a finger tip. The surrounding scalp was not edematous and no hematoma was evident. Roentgenograms of the skull disclosed a round, somewhat irregular, lobular and in places a moth-eaten defect in the right parietal region (fig. 12). It was believed to be an epidermoid.

The patient was operated on December 8 and the incision exposed an area of eroded bone, from which protruded a pulsating bluish mass strongly resembling a hemangioma. It was opened cautiously, and about 1 fluidrachm (3.7 cc.) of old blood escaped. One could then see the typical structure of a dumbbell-shaped epidermoid. The skull was trephined, and a round button of bone which included the skull was removed, at which time the cholesteatomatous material could be seen escaping from the rent in the dura. A small round piece of dura including the rent was then removed. Cholesteatomatous material and old liquid blood came from the subcortical region, leaving a cavity 3 or 4 cm. deep. Around the edges

at the neck of the cavity some lining of the sac could be seen. These edges and the upper part of the wall of the cavity were thoroughly coagulated with the electrocautery. The only other alternative would have been resection of a rather large portion of the brain, which did not seem to be justifiable. Microscopic examination disclosed numerous flat, horny epithelial cells and numerous cholesterol crystals. A pathologic diagnosis of epidermoid was made.

CASE 11.—*Cranial dermoid posterior to the bregma near the longitudinal suture; operative removal and recovery.*

A 38 year old Italian laborer was referred on Jan. 23, 1939, for excision of a tumor of the scalp which was thought to be a sebaceous cyst. This had been present as long as he could remember but had become somewhat larger during the past year.

Examination.—A slightly fluctuant, nontender tumor mass about 3 cm. in diameter was evident to the left of the midline and posterior to the bregma. Roentgenograms of the skull disclosed a saucer-like depression of the outer table just posterior to the bregma and along the longitudinal suture. Preoperatively a dermoid cyst was diagnosed.

On February 2 the cystic tumor was carefully dissected from the depression in the outer table, after which closure was performed without drainage. Dr. Cyril B. Courville described the specimen as a cystic mass arising from a broad base which appreared to be a fibrous membrane. The tumor measured 3.6 by 2.8 cm. in diameter. Sections through the wall

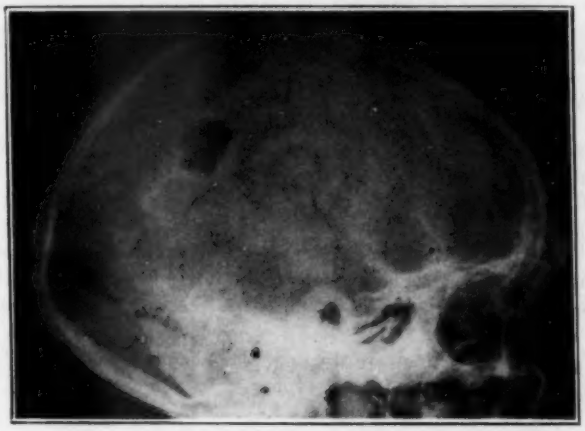

Fig. 12 (case 10).—Lateral roentgenogram of the skull, demonstrating a cranial epidermoid in the right parietal region.

revealed an epithelial lining of squamous to columnar cells with glandular structures in the underlying tissues. The diagnosis was dermoid cyst.

Comment.—That the diploic, or cranial, epidermoids may often be confusing unless one has their identifying roentgenographic characteristics in mind is evident from the 11 cases just presented. So typical is the roentgenographic appearance of the growths that usually the preoperative diagnosis can be established from the films. In spite of this fact these tumors are often undiagnosed. Four of the tumors in our series of cases were operated on as sebaceous cysts. In case 4 four operations were necessary before complete removal was effected. The diagnosis was established only after the roentgenograms of the skull were reviewed. After an incomplete removal of the cyst in case 5, the patient had repeated aspirations for a period of four years. She was then seen by some one familiar with the diagnosis. A review of the roentgenograms taken four years previously revealed the characteristic picture of a cranial epidermoid. Meningioma was thought the most likely diagnosis in case 7. Experience with this case, however, led to the proper diagnosis in case 3, which had not been appreciated when the patient was first seen, five years previously. Because the diploic, or cranial, epidermoids are so easily diagnosed

and can be treated so satisfactorily surgically, it is important that they be recognized before they reach a size which might make complete removal impossible. The importance of this fact is seen in case 9.

B. INTRACRANIAL EPIDERMOIDS AND DERMOIDS

CASE 12.—*Intracranial dermoid cyst in left temporal region; subtotal removal followed by complete extirpation a year later; cerebral abscess and death the following year; autopsy.*

This case was reported previously by one of us.[28] A woman of 40 years was operated on Nov. 11, 1922, at which time the contents of a dermoid were removed from the left temporal region. Marked improvement followed the procedure and continued until recurrence of symptoms became manifest Feb. 1, 1923. Reexploration was carried out February 10, but an attempt to dissect the cyst from the floor of the skull was unsuccessful. Improvement again occurred until the middle of April, when reexploration was again necessary. On April 26 the cyst was emptied of its contents and the entire cyst wall removed. The patient again improved until the following September, when it was necessary to reexplore. At this time no trace of the cyst was found, but a mass about 4 cm. in diameter, which proved to be an abscess, was removed from the left temporal lobe. Cultures were sterile. The patient's condition remained critical. The right hemiplegia and motor aphasia persisted until her death, on March 17, 1924. Pathologic examination of the dermoid cyst showed that its wall resembled true dermis, containing hair follicles, sweat glands and stratified squamous epithelium. The central mass was filled with debris composed of desquamated cells, among which were scattered fine hairs and cholesterol crystals.

CASE 13.—*Parapituitary epidermoid disclosed at operation; partial removal.*

A boy 9 years old was admitted to the hospital June 20, 1928. This case was tabulated as one of postchiasmal cholesteatoma in the third ventricle in a report on tumors of the brain in childhood published by Rand and Van Wagenen[29] in 1935. According to the history the patient had complained of frontal headaches unassociated with nausea or vomiting during the previous five years. His appetite became poor in January 1928, and he lost weight and tended to be listless. Although his eyes were noticeably prominent, his parents were uncertain how long this had been apparent. During the previous year they believed his disposition had changed. He was disobedient, quarreled with other children and seemed to prefer being alone.

Examination.—The patient was a poorly nourished boy of 9 years, who seemed mentally retarded. The fundi showed no indication of pressure. The pupils were equal and reacted well and equally to light and in accommodation. The eyes were prominent. A tendency to internal strabismus, left more than right, was noted. A horizontal nystagmus was present on gaze right and left, and vertical on looking upward. There was a slight left peripheral facial weakness. Hearing was markedly impaired in the left ear, and in the Weber test the sound was referred to the right. Otherwise the cranial nerves disclosed no peculiarities. Coordination tests revealed more or less equal ataxia of the extremities, more noticeable in the legs than in the arms. The Romberg sign was present, the patient swaying in all directions. His gait was ataxic. He staggered in all directions, but somewhat more to the right than in other directions. Deep reflexes were equal and active. Nothing unusual was discovered in the remainder of the neurologic examination. Vestibular examination suggested a lesion of the left cerebellopontile angle or a cerebellar lesion extending into the left angle.

It was believed the patient had a lesion of the posterior fossa, and exploration was advised. He was, however, taken to the Mayo Clinic where Dr. A. W. Adson reported that calcification above the sella turcica was seen roentgenographically. A bitemporal hemianopsia was also discovered, leading to the diagnosis of a supratentorial cyst in the neighborhood of the chiasm. At operation on July 31, 1928, a slightly cystic tumor was discovered, arising in the region of the sella turcica and extending posteriorly into the third ventricle. A portion of the tumor presenting anteriorly to the chiasm was removed and the cyst aspirated, after which an intracapsular enucleation of the lesion was accomplished. The patient made an uneventful recovery.

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28. Rand, C. W.: Intracranial Dermoid Cysts: Report of a Case, with Operative Findings, Arch. Neurol. & Psychiat. **14**:346 (Sept.) 1925.

29. Rand, C. W., and Van Wagenen, R. J.: Brain Tumors in Childhood, J. Pediat. **6**:322, 1935.

Pathologic examination of the tumor tissue disclosed a "calcareocholesteatoma" with a large amount of blood pigment and numerous foreign body giant cells surrounding cholesterol crystals.

Comment.—The case is of interest from the standpoint of diagnosis. Had we appreciated the calcification revealed by the roentgenogram and discovered the bitemporal hemianopsia, the localization would have been established. The importance of appreciating that such chiasmal neoplasms may simulate the signs and symptoms of the more common cerebellar tumors of childhood becomes evident.

CASE 14.—*Epidermoid of the left cerebellopontile angle disclosed at operation and removed subtotally; death four years later.*

A married woman, aged 56, was admitted to the hospital July 8, 1929. During the previous five years she had been troubled with pain in the left side of her head, ringing and deafness in the left ear and numbness and weakness of the left side of the body. During the last two years she had had spells of staggering and falling while walking. The past year she had occasionally regurgitated food through her nose. Diplopia had been present for about three months.

Examination.—Except for obesity the general physical examination revealed nothing noteworthy. The disks were not choked. There was, however, a weakness of the left external rectus muscle, with horizontal nystagmus more marked on gazing to the right than to the left, corneal anesthesia on the left, with diminished pain and touch sensation over the distribution of the left trigeminal nerve, and a slight left lower facial weakness. Hearing was impaired in the left ear with bone conduction greater than air conduction. The pharyngeal reflex was absent, with the uvula pulling to the right. She also had some dysphagia, a slight weakness of the left arm and leg and a slight impairment of sensation over the left side of the body. The Babinski reflex was positive on the left and equivocal on the right. The Wassermann reaction of both the blood and the spinal fluid was negative. Roentgenograms of the skull taken July 10 revealed nothing abnormal. Roentgenograms of the mastoid taken July 12 showed a normal internal auditory meatus with no indication of erosion in the Towne position. The impression was that of a tumor of the cerebellopontile angle on the left side, and exploration was advised. Vestibular tests performed August 10 showed no response from either the horizontal or the vertical canals on the left side and no response from the vertical canals on the right. At this time her gait was markedly ataxic, affecting the left side almost exclusively.

A suboccipital exploration was carried out August 15. Because her condition became rather critical at this time, it was decided to postpone further operation. When the left cerebellar angle was explored, on October 3, a pearly, glistening, irregular-shaped tumor was found. A large amount of cholesteatomatous tissue was removed by subcapsular enucleation. It was not possible to remove the capsule entirely. On June 9, 1930, her condition was reportedly unimproved. She died on Nov. 1, 1933, but autopsy was not permitted.

The surgical specimen was composed of numerous bits of gray, glistening material. Portions of the capsule particularly had a mother-of-pearl luster and were finely nodular. Microscopic examination confirmed the diagnosis of epidermoid.

CASE 15.—*Dermoid cyst between the cerebellar lobes accidentally found at autopsy in a woman of 60 years.*

This woman had been admitted to the hospital several times for bronchitis and for fractures of various bones, the case being reported previously by Courville.[27] She came somewhat irregularly to the hospital for antisyphilitic therapy from 1930 to 1935, and died at home Jan. 13, 1936. Her body was brought to the hospital for examination at the coroner's request.

Dr. Courville, who examined the brain, described a peculiar orange appearance and a granular body in the vallecula of the cerebellum. When the arachnoid was torn this structure appeared as a granular, yellowish body lying beneath the inferior vermis. The tumor mass was friable and granular on section and contained some calcium. The tumor itself appeared to be formed by a cyst, the contents of which were lipoid, containing considerable cholesterol and a few hairs. Microscopically the wall was seen to be composed of dense fibrous epithelium or tissue lined with a layer of stratified squamous epithelium. A number of small calcareous deposits or particles were seen throughout the walls. The wall was intimately attached to the folia in this region. Because of the presence of hair it was felt to be a dermoid rather than an epidermoid cyst.

CASE 16.—*Left-sided convulsions for eighteen years; coma and death following a seizure; autopsy; epidermoid of the right parietal region; acute cerebrospinal (epidemic) meningitis.*

A 58 year old man was admitted to the hospital in coma on Dec. 12, 1932. Left-sided jacksonian attacks had occurred at monthly intervals since 1914. After a severe attack in 1921 he lost control of the lower extremities, bladder and bowels, fair control being restored by the end of a six month period. Two weeks prior to his admission to the hospital he had a mild attack of influenza, and on the night of December 9 a convulsion occurred. The following day he improved, but on the evening of December 11 he became worse, and on December 12 he lapsed into coma.

The past history revealed a gastroenterostomy in 1921 for duodenal obstruction. Shortly after the onset of his convulsive seizures the diagnosis of tumor of the brain was made, but nothing further was done in this regard. He complained occasionally of headache. The past history otherwise revealed nothing of consequence.

Examination.—A complete neurologic examination was not recorded, but it was noted that the pupils were circular and equal and reacted equally to light. The deep reflexes were equal but sluggish, and the Babinski reflex was positive bilaterally. The blood pressure was

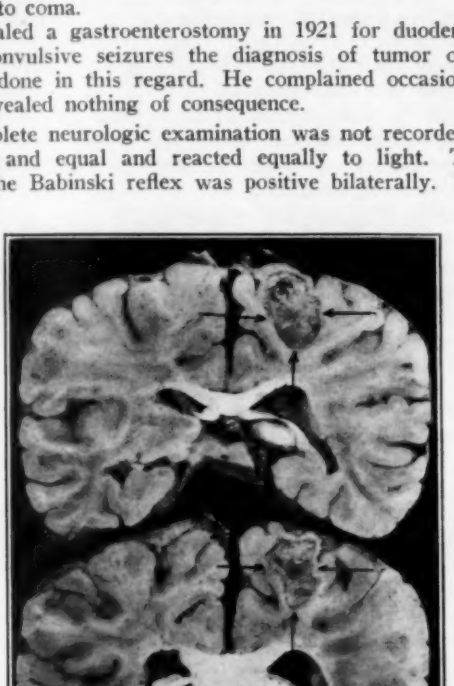

Fig. 13 (case 16).—Photograph of coronal sections of the brain, showing an intracranial epidermoid in the parietal lobe of the right cerebral hemisphere.

150 systolic and 100 diastolic. Urinalysis showed large quantities of albumin, numerous granular casts, occasional hyaline casts and many erythrocytes. The nonprotein nitrogen was 64.5 mg. per hundred cubic centimeters. The erythrocyte count was 4,300,000 and the leukocyte count 17,000.

Autopsy was performed by Dr. J. W. Budd. Gross examination of the brain revealed a thick purulent exudate over the lateral surface of the hemispheres. When the brain was removed a considerable quantity of cloudy fluid escaped from the posterior fossa. The base was covered by a thick purulent exudate which obscured the various vessels and nerves. When the serial coronal sections were made an indurated area 2 by 1 cm. was discovered in the parietal lobe of the right cerebral hemisphere. This subcortical tumor was about 1.5 cm. lateral to the median line. The defect was filled with a yellowish green, gritty material, somewhat inspissated and friable, with tiny glistening spots on the sectioned surface (fig. 13). A smear of the material disclosed many cholesterol crystals. Microscopic examination revealed a cyst wall, the outer part of which was made up of dense glial scar tissue, while the inner part was dense, fibrous scar tissue. This fibrous lining was apparently continuous with the fibrous tissue of the pia at the depth of a sulcus. The cyst contained a granular, structureless form of debris showing many lenticular clefts (cholesterol crystals) and foci of calcification. An epithelial lining was not evident in the microscopic sections. The adjacent cerebral tissue

showed distortion from pressure, with increase of the glial supporting tissue and atrophy of the parenchyma. There was an extensive inflammatory process of the meninges, with exudate consisting largely of polymorphonuclears. When the dura was reflected from the spinal cord, it was found to be covered by a thick veil of yellowish, opaque exudate. Although microorganisms were not seen in the tissue sections, direct smears stained with Gram stain showed intracellular gram-negative diplococci. It was not possible to obtain the organism in culture. Dr. Budd concluded on the basis of the smear findings that acute cerebrospinal epidemic meningitis was the terminal event. There was in addition an epidermoid involving the cortex of the parietal lobe along the right median surface. Additional findings of interest included two diverticula of the intestinal tract and a gastroenterostomy with a small marginal ulcer.

CASE 17.—*Increasing right hemiparesis for five years; roentgenograms revealed a group of calcifications measuring 2 inches (5 cm.) in all dimensions lying within the left middle fossa of the skull; operative removal of a large subdural epidermoid; death and autopsy.*

A married man aged 39, a truck driver, was referred on July 16, 1935. His first symptoms occurred in 1929, with pain in the right forearm radiating down to the hand and up to the shoulder. Later pain was noticed in the right leg. Difficulty in using the right hand, which was observed in 1930, continued and increased. Dragging of the right foot appeared in 1931 and continued thereafter. Increasing numbness of the right side developed. During the past year difficulties in speech occurred, in that sometimes he was unable to talk, although he knew what he wanted to say. There was also difficulty in reading and in writing. During the previous year, and especially during the last three or four months, he had suffered severely with headaches, the pain being mainly in the right occipital region. Since 1930 the patient had had occasional jacksonian seizures involving the right side of the body. Occasionally he was troubled with nausea and vomiting. He had noticed no impairment of vision or hearing, and prior to his present illness his general health had been good.

Examination.—This patient was obviously handicapped by right hemiparesis and by difficulty in speech. Funduscopic examination showed somewhat hazy disk margins with overfilling of the veins, but no measurable elevation. There was a noticeable weakness of the right side of the face, central in character. The visual fields showed no constriction on rough testing. There was a complete astereognosis of the right hand, a right hemiparesis amounting to a complete paralysis of that hand and pronounced weakness of the right side of the face as well as less weakness of the right leg. The Romberg sign was present, the gait being so hemiplegic that the man was barely able to walk. The abdominal and epigastric reflexes were sluggish on the right and active on the left. All of the deep reflexes were hyperactive on the right and active on the left side. Ankle clonus was present on the right and absent on the left. The Babinski reflex and allied signs were positive on the right and negative on the left. The blood pressure was 150 systolic and 90 diastolic.

Roentgenograms of the skull demonstrated a large group of small calcifications, measuring approximately 5 cm. in all three dimensions, lying within the left middle fossa of the skull. The lower margin of this area was about 1 cm. above the level of the clinoid processes.

At operation Aug. 8, 1934, a firm nodular tumor could be felt directly under the dura in the left temporal region. Opening of the dura disclosed a large epidermoid which measured about 8 by 6 by 4 cm. in various diameters. It resembled a potato with nubbins on it. Its contents consisted of a cheesy material which was often pearly white. The tumor had a definite capsule which was thin and had many ramifications. During closure of the wound the patient suddenly died. At autopsy Dr. Cyril B. Courville reported the essential pathologic changes to be in the region of the left sylvian fissure, where two large irregular openings in the membrane were noted, the posterior one measuring 4 by 4.7 cm. in diameter. Beneath the thickened and opaque leptomeninges in the sylvian fissure, the remnants of an epidermoid were observed. Nodules of this tumor were found in the superior surface of the left temporal lobe, while down in the depths of the cavity the tumor was evident in irregular masses. At its greatest depth the cavity actually measured 6 cm. The gross diagnosis was epidermoid (pearly tumor) of the left sylvian region, with operative subtotal removal.

A section was taken from the nodule of the epidermoid still present in the brain. The line between the tumor and the brain was not very distinct, since the superficial cells of the tumor lay in such intimate relationship with the brain substance. These cells, however, were quite characteristic.

CASE 18.—*Large epidermoid in the left cerebellar region; incomplete operative removal; death six days later.*

A 57 year old engineer was examined on Aug. 31, 1936 by Dr. Cyril B. Courville and, in consultation with one of us, on September 2 of the same year. Some twenty years previously the patient had first been troubled with tinnitus in the left ear, which persisted for about seven

years before disappearing. With the onset of the tinnitus his hearing became impaired, and by the time the tinnitus had ceased the left ear was deaf. About 1926 he experienced periodic pain in the occipital region, which he described best as a sense of pressure. With the pressure symptoms he often saw double. In a few months this disappeared, but it returned again during the last few years. About 1927 he noticed short spells of unsteadiness lasting only a few seconds at a time. Two years later they disappeared, and instead there developed a gradually progressive feeling of unsteadiness, particularly in the left hand and leg. In 1932 or 1933 the patient discovered a weakness of the left side of the face which became gradually more pronounced.

Examination.—The fundi were normal. A pronounced weakness of the left external rectus muscle was evident, and the patient saw double when looking straight ahead or to the left. There was a noticeable horizontal nystagmus on looking either to the right or to the left, of wider amplitude on looking to the left but more rapid on looking to the right. The corneal reflex was diminished on the left, and the same was found to be true of sensation over the left trigeminal area. The motor division of the fifth nerve was intact. There was a moderate peripheral weakness of the left side of the face. The ticking of a watch was heard at a distance of 2 feet (60 cm.) from the right ear, but was not heard when the watch was pressed against the left ear. Air conduction was better than bone conduction on the right, but bone conduction was better than air conduction on the left. In the Weber test the sound was not lateralized. The cranial nerves were otherwise intact. Tests for coordination disclosed noticeable ataxia of the left arm and leg. The Romberg sign was present, the patient swaying backward and to the right. He tended to walk on a wide base and was slightly ataxic. Anteroposterior roentgenograms of the skull revealed an erosion of the left porus acusticus internus. It was believed the patient had an acoustic neuroma on the left side.

He was subsequently operated on, November 3, by Dr. H. C. Naffziger, who was surprised to encounter a pearly tumor when he elevated the left cerebellar lobe. He curetted out a large amount of characteristic flaky, white material. The sac had eroded through the bone about midway between the foramen magnum and the tip of the petrous bone. The cyst extended in front of the medulla and then around into the cerebellum and into the left cerebellar tonsil. All possible material was curetted out, and the accessible portions of the capsule were removed. The patient's postoperative condition became critical, and he died six days later.

Dr. Courville reported that the histologic sections presented a classic parallel fibrous structure arrangement, staining feebly. A condensed distended portion, which apparently was the capsule of the growth, stained a bluish pink. The remaining portion of the tissues showed the classic wood fiber arrangement usually found in these pearly tumors.

CASE 19.—*Epidermoid of the right cerebellopontile angle partially removed Dec. 16, 1936; reexploration and complete removal of the tumor Feb. 10, 1937; recovery.*

A married woman of 19 years entered the hospital Dec. 17, 1936, complaining of headaches for two years, progressive unsteadiness of gait for six months, and blurred, failing vision for four months. In 1935 the intensity and frequency of the headaches increased, and they were frequently accompanied by vomiting. During September 1936 her vision began to fail, and by October she was unable to read print. Disturbance of equilibrium was first discovered during July 1936. Gradually she began to stagger more to the right than to the left. This progressed slowly, so that at the time of her admission she could not walk unassisted.

Examination.—The patient was unable to recognize the usual test odors in each nostril. Funduscopic examination revealed bilateral papilledema of 1 to 2 diopters. Her pupils were somewhat dilated and irregular, reacting sluggishly both to light and in accommodation. Nystagmus was noted in all directions, but otherwise the extraocular movements were normal. The corneal reflexes were bilaterally sluggish. Perception of the ticking of a watch seemed diminished in each ear, and perception of sound from a tuning fork was lateralized to the left ear. The remaining tests of cranial nerves gave normal results.

Although well oriented, she was somewhat lethargic and at times facetious. Rough testing of the visual fields suggested concentric constriction. Coordination tests of the upper and lower extremities demonstrated some ataxia bilaterally. The Romberg sign was present. Her gait was ataxic; she fell toward either side. The superficial and deep reflexes were equal and active, the Babinski reflex and allied signs being negative. The blood pressure was 115 systolic and 85 diastolic. Laboratory examinations, including urinalysis and blood count, gave normal results, and the Wassermann reaction of the blood was negative. Roentgenograms of the skull taken Dec. 10, 1936 revealed a slight separation of the sutures. There was also a beaten silver appearance of the skull, and the dorsum sellae showed some erosion.

A suboccipital craniotomy was performed December 16 by Dr. R. B. Raney. A solid tumor was palpable under the dura over the vermis. When the dura was opened a pearly mass was

exposed, overlying the medulla and the vermis. The surrounding capsule was so densely adherent that removal was impossible. It was therefore opened and the white caseous material removed, after which the wall was electrically cauterized and closure carried out in the usual manner.

Dr. Cyril B. Courville reported on a mass of irregular fragments of grayish or pearly white tumor tissue taken from the midline of the cerebellum. The fragments of capsule showed the typical mother-of-pearl appearance. The histologic sections revealed only a small amount of shredded linear material staining pink, which was characteristic of an epidermoid.

The patient returned to the hospital Feb. 5, 1937, unimproved. She was reoperated on February 10, by Dr. Raney, and the remaining capsule, which had been destroyed by cautery during the first procedure, was completely removed. After the second operation she gradually improved. When she was examined Dec. 9, 1938 her vision was steadily improving.

CASE 20.—*Basilar epidermoid in the left frontal region accidentally found at autopsy.*

A white man of 68, a WPA worker, first entered the hospital Feb. 14, 1937, in the medical service, with the history of passing tarry stools two or three days previously. The morning before his admission he fainted and was unconscious for an indefinite period of time. After this he had three episodes of vomiting and lost about a pint of blood. Fluoroscopic examination March 4 revealed an ulcer at the base of the duodenal bulb. Two more or less similar episodes with admission to the hospital occurred March 24, 1937 and May 2, 1939. On the last occasion, however, severe hemorrhage again occurred, which resulted in his death. After autopsy the cause of death was reported as atrophic cirrhosis of the liver, with esophageal varices and massive hemorrhage.

Postmortem examination of the brain revealed a sharply outlined, encapsulated pearly tumor, measuring 2.1 cm. transversely and 2.5 cm. anteroposteriorly, which was embedded in the middle and posterior portions of the basilar surface of the left frontal lobe. Microscopic examination showed it to be an anuclear structure made up of strands and layers of fibrous material. In the examined section none of its peripheral membranes were present, but the study of the section itself strongly suggested the diagnosis of an epidermoid.

CASE 21.—*Epidermoid of the left cerebellopontile angle; death after operation; autopsy.*

A laborer of 41 entered the hospital June 11, 1937, complaining of failing vision since 193[illegible] pain in the back of the head since 1933 and dizzy spells, tremor of the left leg and weakness of the left hand for the past four months. Since 1931 he had been bothered with periods of depression. He volunteered the information that he thought there was "something loose" or a tumor in his head. For some ten years he had noticed increasing impairment of hearing in the left ear, and for four years there had been ringing in that ear.

Examination showed blurring of both optic disks, with numerous hemorrhages in both fundi. Horizontal nystagmus occurred on gaze right and left, and rotary nystagmus on upward gaze. The pupils were circular, equal, and reacted well and equally to light and in accommodation. Marked hypesthesia was noted over the three divisions of the right trigeminal nerve, with absence of the corneal reflex on that side. There was also a weakness of the lower part of the face. By gross testing some impairment of hearing was discovered in the left ear. Speech seemed somewhat thick. Rough testing revealed that the visual fields were contracted moderately. Tests for coordination revealed some ataxia of the upper extremities, particularly the left, but no significant incoordination of the lower extremities. The Romberg sign was absent, and the gait was normal except for a tendency to fall with rapid turning.

Roentgenograms of the skull, including the Towne position, demonstrated no pathologic conditions and showed no evidence of increased pressure. Vestibular tests indicated some impairment of the responses on the left side, and hearing tests revealed some impairment for the higher frequencies. A lumbar puncture yielded spinal fluid with an initial pressure of 350 mm., clear and colorless, with a normal cell count and a negative Wassermann reaction. The Wassermann reaction of the blood was also negative.

Preoperatively it was thought that the patient had a left-sided cerebellar tumor. A suboccipital craniotomy was performed June 23, 1937 by Dr. G. H. Patterson. After the dura was opened and the lateral surface of the left cerebellar lobe removed, a large epidermoid was exposed. It extended into the angle, compromising the seventh, eighth, ninth, tenth and eleventh cranial nerves. By means of a curet and cautery almost all of its contents and capsule were removed. The entire mass seemed the size of a tangerine. The patient's condition was poor. He failed to improve, and in spite of the usual supportive therapy he died that night. An autopsy was performed, and the brain was examined by Dr. C. B. Courville. The specimen consisted of numerous fragments with a nodular surface and mother-of-pearl appearance. Study of a section through one of the fragments showed a narrow remnant of

surface epithelium, forming a dark purple border of the cell. The tissue beneath occurred in the form of a loose parallel arrangement of the strands of structureless material characteristic of the tumor. The microscopic diagnosis confirmed the gross impression of epidermoid.

CASE 22.—*Parapontile epidermoid accidentally found at autopsy.*

A 54 year old woman was admitted to the medical service June 21, 1937. About three weeks previously she had become intoxicated, and as a result she was kept in custody for about five days. Because her condition failed to improve she was transferred to the hospital for diagnosis and treatment. She had had frequent spells of dyspnea and coughing with expectoration of blood-streaked sputum. Roentgenograms of the chest showed abnormal hazy density of almost the entire left pulmonary field, indicating a long-standing intrapulmonary tuberculosis. The Wassermann and the Kahn reaction of the blood obtained June 23, 1937 were negative. Because of the advanced pulmonary tuberculosis the patient was referred to the nearest county tuberculosis clinic.

She was again seen Dec. 29, 1937, when she was brought into the hospital in coma, with the diagnosis of a cerebral accident and a right-sided hemiplegia. Death occurred the following day, and an autopsy was performed by the coroner. His observations included a small extradural hemorrhage and a large subdural hemorrhage over the left frontal lobe of the brain. There was also evidence of old tuberculosis with cavitation in the left upper pulmonary lobe.

In the brain Dr. Cyril B. Courville found moderate thickening of the leptomeninges on the dorsolateral surfaces of the frontal lobes, and the remains of a subdural hemorrhage over the dorsolateral surface of the left cerebral hemisphere. A typical pearly tumor was found, spreading over the base of the pons and medulla and extending into the cerebellopontile angle on each side. The appearance of the tumor was characteristic; it had a brilliant pearly surface and the capsule disclosed a whitish material beneath. Microscopic examination corroborated the gross diagnosis of epidermoid.

CASE 23.—*Parapituitary epidermoid; partial removal and operative recovery.*

A 16 year old high school girl was referred on April 28, 1938. She had noticed loss of vision in the right eye since 1931, and progressive loss of vision in the left eye since March 1938. In 1934 only a slight acuity remained in the right eye. The first intimation of impairment of vision of the left eye occurred during March of 1938, when she discovered she was unable to see as clearly as before. By April 1 she had difficulty in reading, and from that time she felt there had been a slowly progressive impairment of vision. Although the patient was unable to state exactly when her headaches began, she believed they were related to the failure of vision. At first the headache was present every week and seemed to involve mainly the region of the right eye. She recalled that about three years before she had suffered almost daily with headaches over this area. Usually they occurred in the afternoon and lasted a few hours. During the past two years these headaches occurred about twice a week and would last a good part of the day. After the failure of vision in the left eye, she also had some pain in this eye. Occasionally in the last two years she had been somewhat dizzy on getting up in the morning.

The fundi showed an atrophic bluish white disk on the right side. The atrophy of the left disk was more marked on the temporal than on the nasal side. The right eye was blind. With correction the vision in the left eye was 5/15. The cranial nerves were otherwise found to be intact. The left visual field showed a temporal hemianopsia. The rest of the neurologic examination disclosed nothing noteworthy. Roentgenograms of the skull taken April 13 revealed convolutional bony atrophy, suggesting increase in intracranial pressure. The sella turcica was normal. The Wassermann reaction of the blood was negative. The spinal fluid was under an initial pressure of 190 mm. and was clear and colorless; there was no globulin, and the Wassermann reaction was negative.

Ventriculography on May 4 showed nothing significant. In view of the failing vision and the left temporal hemianopsia, a pituitary exploration was performed. Exposure of the sellar region uncovered a glistening mass, the contents of which were the flaky material typical of cholesteatoma. A large amount of this material was removed along with some of the membrane of the cyst. The actual extent of the tumor could not be determined, but it was believed complete removal was impossible.

Dr. R. W. Hammack reported that the specimen consisted of a large amount of gray or pale yellow material. In places the surface was distinctly pearly. Microscopic examination revealed innumerable squamous epithelial cells and a few cholesterol crystals. The diagnosis was epidermoid cyst. Athough the patient has remained well symptomatically, there has been no improvement in her vision. Both optic nerves were bluish white. The visual fields made at this time were essentially the same as those previously taken.

Comment.—In contrast to the diploic or cranial epidermoids, the results with the intracranial epidermoids are far less satisfactory. This is due to the fact that they are less accessible and their capsules may be so intimately associated with vital structures that complete removal is impossible. The 4 cases of epidermoids of the cerebellopontile angle reveal symptoms and signs similar to those of acoustic neurinomas. The epidermoids, however, show a greater involvement of the adjacent cranial nerves than is usual with acoustic neurinomas.

PATHOLOGY

From the time of von Remak's [30] excellent publication in 1854, in which he expressed his opinion that these rare neoplasms resulted from epithelial rests, numerous views have been advanced concerning them. For the most part they have merely corroborated his original conception. Virchow [14] considered all of them due to disturbances of development, and was supported by Mikulicz [31] in 1879 and by Kuster [32] in 1889. He classified them as heterologous tumors arising in the connective tissue. Though it seems evident he regarded them as epithelial, he confused his contemporaries by comparing them with cancroids.

Perls,[33] the first to challenge von Remak's epithelial hypothesis, was of the opinion that these tumors came from the endothelium of the neural lymph spaces; others, including Klebs [34] in 1889, Schmaus [35] in 1895 and Glaeser [36] in 1890, agreed with him. This is more easily appreciated when it is realized that after Müller [13] had devised the term, a variety of tumors came to be called "cholesteatoma" with little regard to their cellular origin, for no other reason than that they contained cholesterol crystals. The interpretation of these tumors became further complicated by the occasional tendency of endothelial growths to copy the structure of cholesteatoma. Such an example is the so-called cholesteatoma of the choroid plexus which Klebs [34] correctly believed to be endothelial in origin. These intraventricular tumors are not comparable to the usual cholesteatoma, and Blumer's [37] term of "cholesteatomatous endotheliomata" is probably quite suitable. Certain of the suprasellar cysts of pharyngeal (Rathke's pouch) origin have similarly complicated the nomenclature. Cholesterol crystals are precipitated in the fluid contents of some of these cysts, and although they undoubtedly originate from epithelial rests dating from an early period of development, these inclusions are of pharyngeal rather than of cutaneous origin and have fluid contents in place of the fatty mass of desquamated cells or cholesteatoma proper.

Critchley and Ferguson [6] felt that in spite of the endothelial theory of Klebs, Perls, Nehrkorn and Kakeshita, they could subscribe only to an epithelial hypothesis for the origin of these tumors. It seemed to them that the most obvious probability was that more than one type of tumor had been described as "cholesteatoma," the

30. von Remak, R.: Ein Beitrag zur Entwickelungsgeschichte der krebshaften Geschwülste, Deutsches Arch. f. klin. Med. **6**:170, 1854.

31. Mikulicz, cited by Kay, F. A., and Pack, G. T.: Cholesteatoma of the Brain: Report of a Tumor of Unusual Size, Arch. Neurol. & Psychiat. **19**:446 (March) 1928.

32. Kuster, cited by Kay, F. A., and Pack, G. T.: Cholesteatoma of the Brain: Report of a Tumor of Unusual Size, Arch. Neurol. & Psychiat. **19**:446 (March) 1928.

33. Perls, M.: Lehrbuch der allgemeinen Pathologie für Studirende und Aerzte, Stuttgart, F. Enke, 1877, vol. 1, p. 486.

34. Klebs, G.: Die allgemeine Pathologie, Jena, Gustav Fischer, 1889, vol. 2, p. 627.

35. Schmaus, H.: Grundriss der pathologischen Anatomie, ed. 9, Wiesbaden, J. F. Bergmann, 1910, p. 241.

36. Glaeser, E.: Untersuchungen über Cholesteatome und ihre Ergebnisse für die Lehre von der Enstehung der Geschwülste, Virchows Arch. f. path. Anat. **122**:389, 1890.

37. Blumer, G.: Bilateral Cholesteatomatous Endotheliomata of the Choroid Plexus, Johns Hopkins Hosp. Rep. **9**:279, 1900.

usual variety being clearly epithelial. The other group which Klebs,[34] Kakeshita [38] and others [6] have described was without doubt endothelial.

Martin, Dechaume and Puig [39] pointed out that the two main possibilities of origin of the epidermoids were that they developed either from a fetal inclusion of epithelial cells or as a result of metaplasia of the endothelial cells of the meninges. Virchow, Eberth and later Glaeser favored the idea of metaplasia. As pointed out by Critchley and Ferguson,[6] however, if the metaplasia theory were correct, one would expect to find transition forms between the epithelial and the endothelial elements in the same tumor, something they were unable to demonstrate. In agreement with most others, they expressed the opinion that these neoplasms occurred as a result of a fetal inclusion of epidermal cells, which, depending on the depths of the layer or according to the embryonic age, produced either an epidermoid or a dermoid type of tumor.

Closure of the medullary groove occurs at the beginning of the third week of fetal life, when constrictions appear in the formation of the three primary cerebral vesicles. Most writers accept Bostroem's conception that misplaced cells from the dermal or epidermal anlage give rise to the dermoid or epidermoid tumors found in the midline of the brain. During the fourth and fifth week, when the secondary vesicles are developing in the forebrain and the metencephalon and the myelencephalon are becoming differentiated in the hindbrain, cell rests that are misplaced may lie away from the midline.

Such hypothesis affords a reasonable and adequate explanation for the occurrence of the majority of epidermoids: those, in other words, arising from the basal excavation of the brain. It does not, however, account for the origin of the intracerebral tumors and the intradiploic and the cholesteatomatous growths within the spinal canal. However, there seems no reason why the same factor of cell inclusion is not similarly tenable. Critchley and Ferguson [6] pointed out, moreover, that the explanation of the occurrence of epithelial elements in association with the membranes become intelligible. This is based on the investigations of Harvey and Burr [40] on meningeal development, in which they demonstrated that certain ectodermal elements, derived in large part from the neural crest, are contributed to the mesenchyme and take part in the formation of the leptomeninx.

The cholesteatomatous masses associated with chronic suppurative conditions of the middle ear have generally been considered entirely different lesions. They result from a chronic inflammatory desquamative process and are not neoplastic as are the true dermoids. In contradistinction to the primary or true tumor, this secondary type of cholesteatoma has also been called caseous metamorphosis, inflammatory cholesteatoma and cholesteatosis.

Wingrave [41] expressed the belief that the cholesteatomatous formation in the ear occurred after prolonged persistence of perforations of the tympanic membrane, as a result of the replacement of the normal epithelium of the middle ear by squamous epithelium. It was his opinion that this metaplasia involved not only the tympanum but the adjacent pneumatic spaces as well and that the rapidly growing new epithelium accumulated because cytolysis and disposal were difficult. Variations of this theory have been expressed by numerous otologists.

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38. Kakeshita, T.: Zur Pathologie der Hirn-Cholesteatome, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **27**:327, 1925.

39. Martin, J. F.; Dechaume, J., and Puig, R.: Morphologie et histogénèse des tumeurs méningées craniennes, Ann. d'anat. path. **5**:277, 1928.

40. Harvey, S. C., and Burr, H. S.: Development of the Meninges, Arch. Neurol. & Psychiat. **15**:545 (May) 1926.

41. Wingrave, V. H. W.: Notes on the Pathogeny of Cholesteatomata, J. Laryng. **25**: 339, 1910.

Those favoring metaplasia of the mucous membrane of the middle ear as the explanation of this problem have not been without criticism. One of the main difficulties has been to account for the manner in which a tumor composed of stratified and horny epithelial cell elements might arise in a cavity lined with columnar epithelium. It has also been pointed out that mere epidermal invasion of the middle ear is not sufficient to cause cholesteatomatous growth. As early as 1878 Schwartze [42] described epidermic blind pouches jutting into the middle ear and persisting throughout life without tumor formation. Rare cases, moreover, have been reported in which no perforation of the ear drum was demonstrable through which epidermal invasion could take place. It was probably for this reason that the theory of metaplasia of the antrotympanic membrane arose. Such a cholesteatoma usually follows marginal rather than central perforations of the eardrum. Wingrave [41] has compared the mechanism with the well recognized phenomenon in which rectal and nasal polyps undergo transformation of their surface into a stratified or horny type of tissue when they protrude permanently from their orifices.

Another type of cholesteatoma rather infrequently encountered by otologists is that variety originating within the mastoid air cells, one which apparently develops without the necessity of either tympanic perforation or sepsis. Lucae [43] in 1873 was one of the first to record a cholesteatoma arising in the mucous membrane of the tympanic cavity with no evidence of perforation of the eardrum nor any indication of aural disease.

Cushing [44] was of the impression that many of the cholesteatomas reported by otologists were true epidermoid tumors, originating from aberrant epidermal rests laid down in the temporal bone during the early formation of the complicated special sense organ it contains. He expressed the opinion, moreover, that it was not improbable in many of the recorded cases that the cholesteatoma itself was responsible for the otitis media, rather than the reverse. The possibility that the cholesteatomas of the petroas and of the mastoid are merely examples of the larger class of diploic or cranial epidermoids merits further consideration and investigation.

Ordinarily the gross appearance of an epidermoid is so characteristic that a correct pathologic diagnosis can be rendered at sight. So striking is the glistening white capsule that it has seldom failed to impress the observer. Often the contents of the epidermoid tend to fragmentation, although caseation and necrotic change may occur in tumors of long standing. The dermoids, on the other hand, are often soft with cystic consistency. Although they frequently have a pearly sheen, their color is more likely to be an opaque yellow. The presence of sebaceous material, fat and cholesterol crystals in varying proportions determines the consistency of the dermoids, and usually they contain hairs, coiled, clumped or matted together. It has been considered that the presence of hair may be regarded as pathognomonic of the dermoid or teratoid type of growth. On cross section an epidermoid has a uniform consistency and contains a finely granular, white or creamy yellow material which tends to be laminated. If the section is made in another plane, it has a concentric laminated appearance not unlike that of an onion. The surface of the tumor, moreover, has a soapy or waxy quality. The absence of vascularity is a noteworthy feature of the epidermoids. In most cases a definite point of attachment and a more or less intimate association with the pia-arachnoid are demonstrable.

42. Schwartze, H.: Pathologische Anatomie des Ohres, Berlin, A. Hirschwald, 1878.
43. Lucae, J. C. A. L.: Arch. f. Ohrenh. **1**:225, 1873.
44. Cushing, H.: A Large Epidermal Cholesteatoma of the Parietotemporal Region Deforming the Left Hemisphere Without Cerebral Symptoms, Surg., Gynec. & Obst. **34**:557, 1922.

Histologically there is a close resemblance between the dermoids and the epidermoids, but, as the name implies, the epidermoids consist only of ectodermal derivatives, while the dermoids are characterized by ectodermal epidermis plus mesodermal corium with its connective tissue, fat cells, sebaceous glands and hair follicles. The dermoids consist of a fibrous outer layer, a connective tissue stroma and an epithelial inner layer. The connective tissue matrix or corium may contain sebaceous glands, hair follicles, fat cells, smooth muscle, elastic fibers and blood vessels. Calcification and bony or cartilaginous spicules may occur in the connective tissue matrix and be visible roentgenographically. Although histologically the epidermoids are usually composed of four concentric layers of different thickness, named the stratum durum, the stratum granulosum, the stratum fibrosum and the stratum cellulosum, each of these may become detached and lie free. For this reason they are difficult to fix and section, and the microscopic picture often is ragged and fragmentary. The more external stratum durum, the layer responsible for the pearly sheen, is made up of layers of collagen fibers with little or no trace of cellular formation. The underlying stratum granulosum, essentially a cellular layer composed of stratified to cuboidal epithelium, corresponds with the dermis. Its typical cell is a comparatively large, oval or circular structure with a large rounded nucleus, both of which stain intensely blue with iron hematoxylin. Throughout the cytoplasm are scattered fine granules of keratohyalin, which in the deeper layers of the stratum become larger and more numerous. Between the stratum granulosum and the deeper layers of the tumor, there is usually a sharp line of demarcation and even an actual gap. Although the stratum fibrosum and the stratum cellulosum are the innermost zones of the neoplasm, a clear differentiation between these two strata is often not possible, for the tissue underlying the stratum granulosum seems to pass by gradual transition into the main central mass of the epidermoid. These layers bear some resemblance to the stratum durum and are made up of loosely packed layers of wavy, homogeneous laminas with the staining properties of keratohyalin. It has been felt that a more appropriate name for the tissue constituting the bulk of the tumor would be "area cornea," because of its similarity in appearance and in chemical properties to the most superficial elements of the dermis. In the area cornea are the retention products of cast-off dead and horny scales. The presence of cholesterol crystals is accounted for by the breakdown of keratin and keratohyalin. There is a striking absence of vascularity throughout the whole of the tumor.

With the exception of the cerebellopontile angle and the diploic areas of the skull, the ordinary situations of the dermal and of the epidermal cholesteatomas are similar. They arise for the most part from the subarachnoid cistern somewhere near the midline at the base of the brain or in the region of the fourth ventricle. While one of the most common places for the non-hair-containing variety is in the cerebellopontile angle, few dermoids have been reported in such locations. As Bucy [45] has pointed out, epidermoids may arise beneath the scalp, within the diploe, between the bone and the dura mater and beneath the arachnoid membrane. The less common, slowly accumulating epidermoids between the inner and the outer table of the skull, the intradiploic type, may attain great size and markedly deform one of the cerebral hemispheres without giving neurologic evidence of their presence.[24] On the other hand, few diploic dermoids have been reported. In the growth of an extradural, intradiploic cholesteatoma, the tables of the skull are pushed apart, with absorption of either the inner or the outer table or both, the

45. Bucy, P. C.: Intradiploic Epidermoid (Cholesteatoma) of the Skull, Arch. Surg. **31**: 190 (Aug.) 1935.

inner table as a rule being more affected. The result is a fairly characteristic roentgenographic picture, with a clear line of demarcation caused by a ridge of the bone forming a rim around the margin of the growth.

The dermoids are usually much larger than the epidermal tumors and have a tendency to push into one or the other cerebral hemisphere, especially in the temporal lobe. They are also much more apt to be cystic and are more frequently single than are the epidermoids.

According to Frank,[46] in the case recorded by Ladame in 1890 three tumors occurred, two in the lateral ventricle attached to the corpus callosum and another nearby. The first reported epidermoid of the spinal cord, that described by Eppinger[47] in 1875, was one of multiple tumors of the cord and brain growing in relationship with the blood vessels. In Trachtenberg's[48] case reported in 1898 there were multiple arachnoid epidermoids and dermoids of the cervical, dorsal and lumbar portions of the cord. Cholesteatomas were likewise found in the left sylvian fossa, in the left frontal lobe, in both lateral ventricles, in the choroid plexuses of the lateral and third ventricles and in the corpora quadrigemina. Microscopically he found them to resemble the tumors described by Bostroem.[2] Other examples were published in 1903 by Ivanoff[49] and in 1904 by Raymond, Alquier and Courtellemont.[50]

With the exception of the diploic epidermoids, the diagnosis and localization of these tumors depend on the same methods used for other intracranial neoplasms. In spite of the fact that the roentgenographic picture of the diploic, or cranial, epidermoids is strikingly characteristic, these tumors are frequently operated on as sebaceous cysts. This is probably accounted for by the fact that the roentgenographic appearance and pathologic characteristics of these tumors are relatively unknown. Lowe and Kernohan[21] have pointed out that sebaceous cysts of the scalp should be distinguished from epidermoid tumors situated between the scalp and the skull, the greatest difference being an absence of squamous epithelium and of keratohyalin granules and the presence, instead, of a secreting type of epithelium in the former.

Of our series of 11 diploic epidermoids, only 4 were properly diagnosed when first seen. Three of the patients were operated on elsewhere. One of these epidermoids, which had been operated on several times without complete removal, showed suggestive malignant change, sufficient to give the appearance of a squamous cell carcinoma.

As has been emphasized by Cushing,[44] Bucy,[45] King[24] and others, it is important that the wall of the cyst, which is the only living, growing part of the neoplasm, be completely removed. This must be done to prevent recurrence; simple evacuation will not suffice. Because the diploic epidermoids are easily diagnosed, are accessible surgically and usually can be removed entirely, it is important that they be recognized before they reach a size which might make complete removal impossible. A good illustration of the importance of this is evident in case 9.

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46. Frank, C.: Ueber einen in der Duerener Irrenanstalt beobachteten Fall von Cholesteatom, Allg. Ztschr. f. Psychiat. **46**:30, 1890.

47. Eppinger, H. E.: Mitteilungen aus dem pathologischen anatomischen Institut, Prag., Vrtljschr. f. d. prakt. Heilk. **133**:126, 1875.

48. Trachtenberg, M. A.: Ein Beitrag zur Lehre von den arachnoidealen Epidermoiden und Dermoiden des Hirns und Rückenmarks, Virchows Arch. f. path. Anat. **154**:274, 1898.

49. Ivanoff, N. S.: Cholesteatom des Rückenmarks, J. nevropat. i psikhiat. Korsakova (supp.) **3**:80, 1903.

50. Raymond, F.; Alquier, L., and Courtellemont, V.: Un cas de kyste dermoïde des centres nerveux, Rev. neurol. **12**:635, 1904.

Results with the intracranial epidermoids are far less satisfactory. Although, again, complete extirpation should, if possible, be undertaken, often intracapsular enucleation is all that can be accomplished. When the capsule remains recurrence is likely, for it is the capsular portion which constitutes the active, growing portion of the tumor. Because of the neoplasm's avascularity, the contents and capsule occasionally can be removed. Not infrequently, however, the tumor may spread rather extensively along the cisterna interpeduncularis and into the region of the third ventricle. A portion of the capsule may be intimately associated with such structures as the optic nerve or the vessels of the circle of Willis. In such instances complete removal is out of the question.

SUMMARY

Dermoid and epidermoid tumors (cholesteatomas) of the central nervous system are uncommon, slowly growing neoplasms representing epiblastic inclusions of the dermal and epidermal layers. The intracranial variety is seldom diagnosed preoperatively. The extradural, or diploic, type can be recognized roentgenographically.

The diploic type is easily accessible surgically, and postoperative results are exceptionally good. Sebaceous cysts of the scalp can be distinguished pathologically from epidermoid tumors by the absence of squamous epithelium and of keratohyalin granules and the presence, instead, of a secreting type of epithelium in the former. The fact that such epidermoids are sometimes overlooked may be given as the reason that Mahoney [3] was able to find only 23 diploic epidermoids in the series of 142 which he collected from the literature in 1936.

Although complete extirpation of these tumors is necessary to prevent recurrence, this often cannot be accomplished in the cases of intracranial epidermoids, because of their extent and attachment to vital structures. The epidermoids of the cerebellopontile angle show signs and symptoms similar to those of acoustic neurinomas, with the exception that there seems to be a greater involvement of the cranial nerves on the affected side.

The use of the words "epidermoid" and "dermoid," suggesting their origin, seems the most satisfactory terminology for these tumors. The term "cholesteatoma" is an unfortunate designation, for the reason that it refers to a chemical by-product which is neither an essential nor an invariable constitutent of these tumors.

The history, incidence and pathology of these neoplasms are discussed.

SO-CALLED "BENIGN METASTASIZING GOITER"

REPORT OF TWO CASES WITH INTRACRANIAL METASTASIS

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Medical literature contains numerous references to so-called "benign metastasizing goiter" and to "metastasizing normal thyroid tissue." Attention was first drawn to this condition by Cohnheim,[1] who reported such a case in 1876. Many reports have since appeared. In 1926 Simpson [2] reviewed the literature and collected 77 cases. Since that survey 28 additional cases have been reported in the literature.

The ability of tumors to metastasize at a distance has been generally considered a cardinal criterion of malignancy. Nevertheless certain primary benign neoplasms, chiefly those of connective tissue origin, such as lipomas, myxomas and chondromas, are capable of widespread dissemination. Generalization of benign epithelial tumors, on the other hand, rarely if ever occurs.

According to the literature, adenoma of the thyroid gland apparently forms an exception to the rule of nonmetastasization of benign epithelial tumors. Cases of simple adenoma, of hyperplastic goiter and even of normal thyroid tissue with single or multiple implants in distant organs have been reported. Much controversy has raged over this fact, with conflicting opinions as to whether such a situation can exist.

Cruickshank,[3] Symmers,[4] Ginsburg [5] and others have favored the theory of benign metastasis. According to Cruickshank:

> A normal thyroid, a colloid thyroid, a thyroid containing a small adenoma, a thyroid containing a malignant adenoma, each has at some time or other been reported as having produced a metastasis consisting of normal thyroid tissue. . . . The clinical fact, or observation, remains that tumours identical with normal thyroid tissue do occur in bones of patients who present no apparent abnormality of their thyroid glands.

Ginsburg, who made a study of metastasis from thyroid tumors to bone, cited a number of cases in support of his contention that metastasis to bone is of frequent occurrence, not only with carcinoma and sarcoma but with simple adenoma of the thyroid gland. He also stated that bulky metastatic tumors of bone, single or multiple, may arise not only from a large primary lesion but from a small, symptomless and histologically benign simple adenoma of the thyroid gland and that even a malignant metastatic tumor may arise from a benign primary adenoma. Symmers [4] regarded some of these metastases as representing aberrant thyroid anlages which may occur in various parts of the body, including the meninges. Though the tumors are histologically benign, he admitted their ability to assume malignant potentialities, in that they may set up secondary deposits in distant structures.

From the Divisions of Neurosurgery and Thyroid Surgery and the Department of Pathology of the Jewish Hospital.

1. Cohnheim, J.: Einfacher Gallertkropf mit Metastasen, Virchows Arch. f. path. Anat. **68**:547, 1876.
2. Simpson, W. M.: Three Cases of Thyroid Metastasis to Bones, Surg., Gynec. & Obst. **42**:489, 1926.
3. Cruickshank, M. M.: Thyroid Metastasis in Bone, Indian M. Gaz. **73**:656, 1938.
4. Symmers, D., cited by Kaplan, I. I.: Benign Metastatic Bone Involvement from Thyroid Tumors, Am. J. Surg. **23**:559, 1934.
5. Ginsburg, S.: Bone Metastasis of Thyroid Tumors, Am. J. Roentgenol. **17**:203, 1927.

The opposing view, namely that so-called "benign metastatic thyroid nodules" represent secondary implants from a primary carcinoma of the thyroid gland, is now favored by most authorities. Simpson has been the chief protagonist of this viewpoint, and he has been supported by Shields Warren,[6] Graham[7] and others.

Careful analysis of the cases in the literature reveals that in most instances the diagnosis was based on the clinically benign appearance of the goiter of the thyroid gland and on the benign microscopic appearance of extirpated metastases. In only 29 of the 77 cases studied by Simpson were there microscopic examinations of the thyroid gland, and in many of these there were areas of undoubted carcinoma which went unrecognized. In most instances the authors published case reports shortly after they discovered the innocent microscopic appearance of the metastases without waiting to learn the ultimate fate of the patient. Patients with so-called "benign metastasizing goiter" have many years later died from frank carcinoma of the thyroid gland. Simpson cited 3 cases of his own in point which clearly illustrate the truth of this contention. Many cases are recorded in which the microscopic examination of the tissue from the metastases revealed normal thyroid structure while subsequent histologic study of the thyroid gland itself showed areas of undoubted carcinoma. A similar situation applies to the recently reported cases as well. All in all, therefore, very few of the reported cases can be accepted as instances of "benign metastasizing thyroid tumor." The evidence in these cases rests on the study of the thyroid gland as well as of the metastases. That benign thyroid tumors can metastasize at a distance is postulated on evidence that other primary benign neoplasms are capable of distributing secondary implants at a site removed from the primary lesion.

PATHOGENESIS

Of interest are the theories which have been invoked to explain the pathogenesis of this condition.

One theory is that metastases represent misplaced embryonal cells or aberrant thyroid tissue. This is the view held by Ewing,[8] who stated: "In explanation of these cases it seems necessary to assume an origin either from aberrant thyroid tissue or from dislodged cells from the normal thyroid." However, he cautiously added: "Yet in none of these cases has the supposed normal thyroid been submitted to microscopical examination." The presence of multiple widely disseminated foci of thyroid tissue in areas where aberrant thyroid tissue could not possibly occur also invalidates this argument.

A second explanation is that normal thyroid tissue, because of its close relationship to blood and lymph channels, may break into the blood stream, be carried to bone and set up a new growth, bone forming an excellent medium for the growth of thyroid cells. This theory also appears illogical, for if normal thyroid cells possess the power to proliferate in a favorable environment, such as bone, it is strange that artificial autoplastic implantations of thyroid tissue in long bones have not been followed by such proliferative and destructive growth. Then, too, if normal thyroid cells possess such an unlimited capacity for growth in distant organs, it seems remarkable that metastases should occur so infrequently.

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6. Warren, S.: Significance of Invasion of Blood Vessels in Adenomas, Arch. Path. **11**:255, 1931.

7. Graham, A.: Malignant Epithelial Tumors of the Thyroid, Surg., Gynec. & Obst. **39**:781, 1924.

8. Ewing, J.: Neoplastic Diseases, ed. 4, Philadelphia, W. B. Saunders Company, 1940, p. 987.

The third and most likely view is that the goiter which gives origin to metastases ought not to be considered a benign tumor and that the metastatic tumors arising from it, even though histologically not malignant, should be considered as such.

The evidence for this third view is as follows:

1. The vast majority of reported cases cannot be accepted because only a few of the so-called "normal thyroids" or "benign goiters" have been submitted to microscopic examination and only a few of the thyroids examined histologically have been studied adequately to rule out malignancy.

2. The metastases of so-called "benign goiters" show the same predilection for bone that characterizes secondary carcinomatous implants. The cranial bones, the sternum, the verebral bodies, the humerus and the femur are the most frequent sites, in the order named.

3. According to the opinion of the most authoritative pathologists, the morphologic character of the tissue is an unreliable basis for the determination of malignancy of thyroid epithelial tumors. There is even considerable variation in architecture in a single portion of normal thyroid tissue.

Graham [7] categorically stated: "Epithelial tumors of the thyroid gland that are encapsulated and show no blood vessel invasion are benign irrespective of their microscopic picture. Epithelial tumors that invade the capsule or blood stream are malignant irrespective of the microscopic appearance." Furthermore, the primary malignant lesion in the thyroid may be miniature and escape clinical and even microscopic detection unless serial sections are made.

CLINICAL FEATURES

Clinically, these lesions are insidious in onset and do not present symptoms different from those of other tumors of bone. However, two interesting observations that are of diagnostic importance are the presence of palpable and often visible pulsations synchronous with the pulse and the tendency of the metastases to fluctuate in size during menstruation and pregnancy. Pulsation is especially common in cranial metastases, and a bruit is not infrequently audible over the mass. Another interesting feature is that the metastatic implants may function, with resultant hyperthyroidism. Oddly enough, removal of the primary lesion rarely produces changes in symptoms, but removal of the secondary growth may cause relief of symptoms and even myxedema.

The true nature of the lesion remains unsuspected as a rule until the pathologist has reported his observations. According to Zadek,[9] approximately 38 per cent of the bone metastases are in the cranium and 15 per cent in the verebrae. Two thirds to three quarters of the patients are females. The average age is 40 to 60 years. The condition is often of many years' duration.

TREATMENT

Concerning treatment, radical surgical removal of metastatic thyroid tissue if accessible, as well as of the primary tumor, is indicated, especially because of the almost universal and sometimes fatal recurrences. Fortunately these are not apt to appear until several years has elapsed. In some of the reported cases extirpation of the metastatic tumor resulted in permanent cure. This is the exception rather than the rule. Roentgen therapy to the site of metastatic implants and to the

9. Zadek, I.: Pathological Fracture of Neck of Femur Due to Thyroid Metastases, Ann. Surg. **77**:689, 1923.

thyroid gland itself is indicated whenever possible, because of the radiosensitiveness of these neoplasms.

Two illustrative cases are reported.

REPORT OF CASES

M. S., a 51 year old housewife, was admitted to the Jewish Hospital of Brooklyn, service of Dr. Leo M. Davidoff, on Jan. 25, 1942, because of progressive exophthalmos in the right eye of three months' duration. There was some blurring of vision of the right eye on occasions,

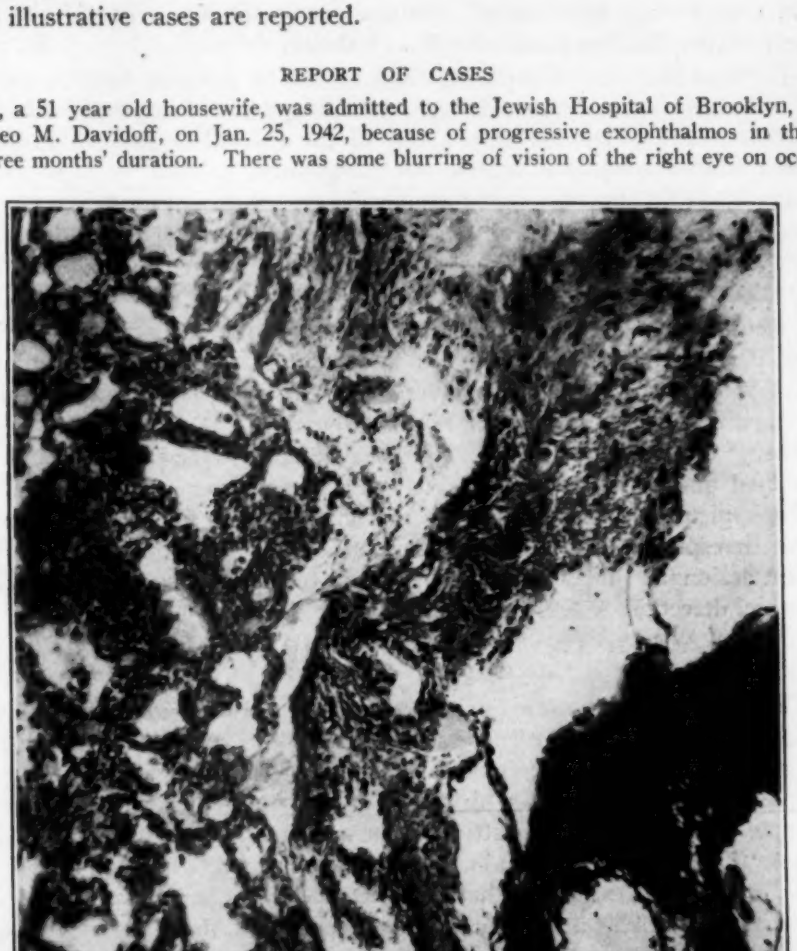

Fig. 1 (case 1).—Thyroid tissue in temporal bone resembling benign adenoma with destruction of bone (hematoxylin and eosin stain; × 250).

especially during reading, but no other visual symptoms. She had suffered from migraine during the past thirty years. Otherwise her past history was irrelevant.

Significant findings on physical examination were limited to the eyes. There were exophthalmos and defective abduction and elevation of the right eye, slight dilatation of the right pupil and slight pallor of the extreme temporal margin of the right optic disk. The visual fields were normal. The neurologic examination gave entirely negative results.

Roentgenograms of the skull revealed a destructive process involving the right sphenoid ridge and the posterior portion of the right orbit with marked decalcification. Along the outer portion of the ridge, adjacent to the skull table, was a calcific deposit, believed to be part and parcel of the tumor mass. Both optic foramens were normal. These observations

were considered as consistent with the diagnosis of a tumor in this region involving the skull, possibly a meningioma of the sphenoid ridge.

Operation was accordingly performed on January 27 by Dr. Davidoff. It revealed an extensive, exclusively extradural tumor involving the squamous portion of the temporal bone, the lesser wing of the sphenoid and the orbital roof and fascia on the right side. In places the tumor had eroded through the temporal bone and made its way into the temporal fossa beneath the temporal muscle. It was felt that the tumor was either a meningioma or a sarcoma. A total gross removal of the tumor was carried out.

The patient seemed to be in fairly good condition for about thirty-six hours after the operation. She then began to complain of pain in the face and in the right eye and became drowsy slowly. The drowsiness increased, and she eventually became comatose. Her right

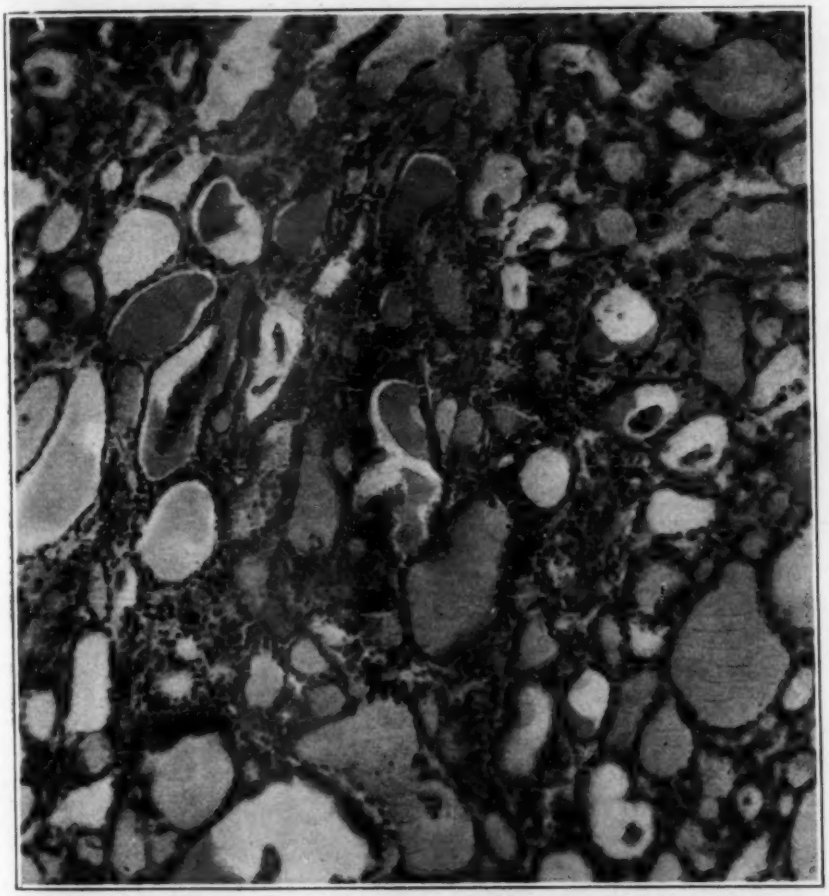

Fig. 2 (case 1).—Section from thyroid gland with fetal adenoma (hematoxylin and eosin stain; × 250).

pupil became dilated as compared with the left, her pulse became slower and her blood pressure rose. A diagnosis of extradural hematoma was made. Immediate operation was performed; the diagnosis was verified, and the freshly accumulated extradural clot was evacuated through the operative site. Thereafter she made slow but steady progress and her course was uneventful. The exophthalmos receded considerably.

To the amazement of every one concerned, the tumor was reported histologically as composed of thyroid gland tissue (papillary adenoma), evidently metastatic (fig. 1). There was no histologic evidence of malignancy, nor were tumor cells seen within blood vessels. Careful reexamination of the patient then revealed a small nodule in the left lobe of the thyroid gland. It was felt that the metastatic deposit probably arose from this nodule, and its removal was deemed advisable. The basal metabolic rate as determined on February 13 was reported to

be + 19; however, the patient was extremely restless on that day and the report was considered unreliable, especially since her basal metabolic rate prior to admission was reported as normal by the family physician.

On February 18 subtotal thyroidectomy was performed by Dr. H. Louria. The thyroid gland weighed 23 Gm. The left lobe contained two well encapsulated nodules, the larger of which measured 3 cm. in diameter. The left lobe contained a solitary small nodule. All resembled fetal adenomas. Histologically the thyroid gland and the adenomas appeared benign, with orderly arrangement of cells (fig. 2). No evidence of intracapsular extension or invasion of blood vessels was found. The microscopic diagnosis was adenomas of the thyroid gland.

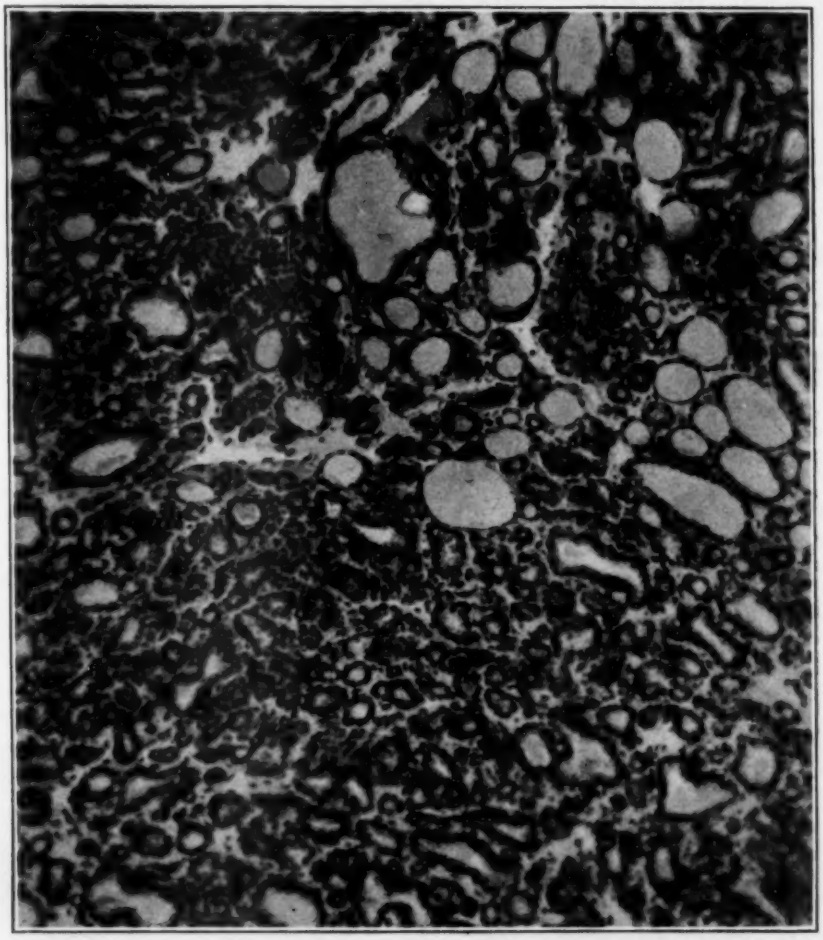

Fig. 3 (case 2).—Section of tumor from frontal bone resembling fetal adenoma (hematoxylin and eosin stain; × 250).

The patient was discharged on February 20, evidently having made a satisfactory recovery from both operations.

Laboratory data were essentially within normal limits.

The patient is now receiving roentgen therapy to the skull and neck, and thus far there is no evidence of recurrence or further metastases.

The final diagnosis was so-called "benign metastasizing goiter" with metastases to skull and probably carcinoma of the thyroid gland.

Case 2.—D. J., a 57 year old Jewish housewife, was admitted to the Jewish Hospital of Brooklyn, service of Dr. Leo M. Davidoff, on March 19, 1942, because of a lump on the right

side of her skull in the frontal region. The lump had been present for a year, but she had paid little attention to it until shortly before admission, when she noted that it had become progressively larger. She also noticed the presence of a dilated blood vessel in proximity to the mass and was aware of pulsation of that vessel. She said she had not felt any pain in this region, and neurologic inquiry gave negative results. She had had a laparotomy thirty-four years previously, reportedly for an "abscess," and had known of a lump in her neck for twenty years. Two days before admission she came to the outpatient department and was told she had a cyst and advised to return on the day of admission for excision of the mass. This was attempted with local anesthesia, but after the initial incision had been made unusual

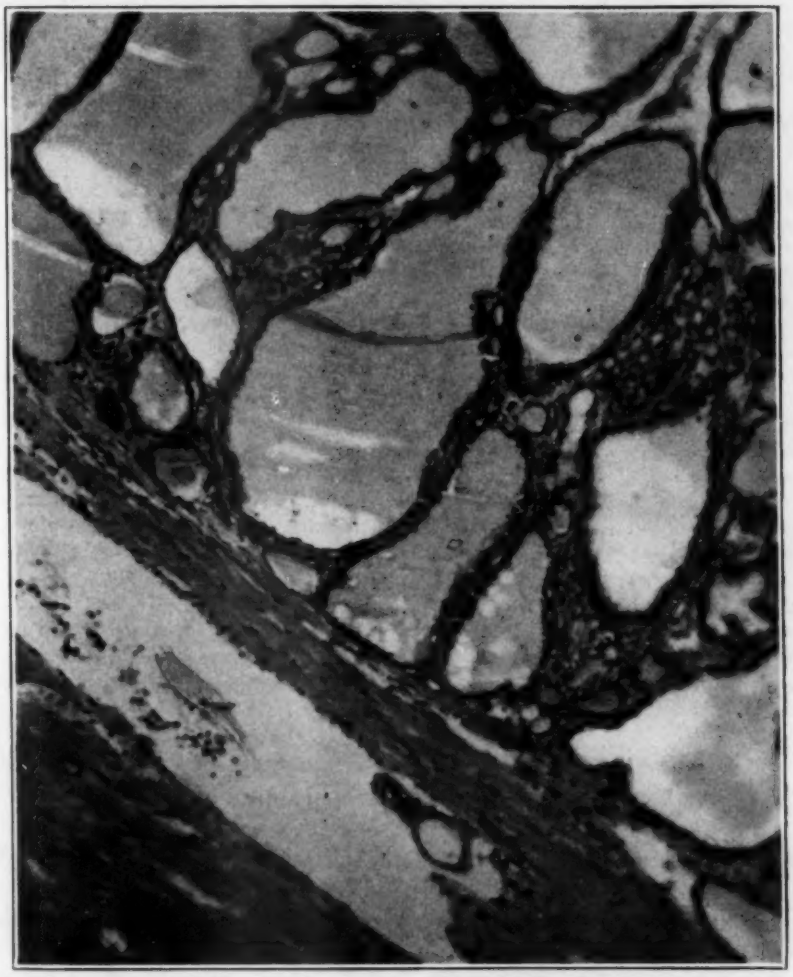

Fig. 4 (case 2).—Section with thyroid tissue in lumen of vein in thyroid gland.

vascularity and pulsation of the mass were noted. The wound was immediately sutured, and hospitalization was advised.

When the patient was admitted to the hospital a plum-sized mass over the right frontal area pulsated visibly. A bruit was readily audible over the right frontotemporal region, and a greatly dilated temporal arterial vessel was noted. It was the opinion of one examiner that pressure over the right carotid artery caused the mass to cease pulsating and obliterated the bruit. The thyroid gland presented a bilateral nodular enlargement. The right lobe was somewhat larger than the left. According to the patient, the mass in the right lobe was of recent origin and the nodule in the left lobe was of many years' duration. Both lobes, however, were movable and did not appear to be adherent to the underlying tissue. Clinically the

thyroid gland did not appear to contain any malignant growth. A suprapubic incisional hernia and advanced bilateral varicosities of both lower extremities were noted.

Roentgenograms of the skull showed a large defect in the right frontal bone, measuring 5 by 4 cm., with irregular, serrated edges. There was considerable increase in the number of vascular channels inferior to the lesion.

The patient was discharged on March 24 and advised to return when the cutaneous incision made when she was being treated in the outpatient department had healed.

She returned on May 4. Operation was performed on May 6 and revealed a pink-gray, meaty, vascular friable mass deep to the pericranium in the right frontal region with a bony defect. A frozen section of biopsy material from the tumor was reported as benign thyroid adenoma. The tumor was partially resected with the electrocautery. Hemostasis was obtained with difficulty.

Grossly, the tumor consisted of a spherical mass of tissue which weighed 22 Gm. and measured 5.3 by 5 by 1.7 cm. One surface appeared smooth and glistening and was pink-gray; the other surface was fairly homogeneous, dry and opaque. In places the tumor had a lobulated appearance. The central portion was dense and firm. Microscopically the tissue resembled a simple adenoma of the thyroid gland (fig. 3). It betrayed none of the characteristics usually associated with malignant growth.

The wound healed per primam intentionem. Roentgenograms of the long bones, the spine and the chest failed to disclose any evidence of metastatic malignant growth. Her basal metabolic rate was +7. It was felt that this case also was one of so-called "benign metastasizing goiter," and removal of the primary growth was deemed advisable. Subtotal thyroidectomy was accordingly performed on May 20, with local anesthesia.

Grossly the thyroid gland weighed 70 Gm. and measured 8 by 6 by 4 cm. The entire specimen consisted of two distinct encapsulated nodules attached to one another by a thin bridge of thyroid tissue. The consistency of the tissue was firm; calcification was noted in some areas. The cut surfaces of the larger nodule presented central areas of cavitation with fresh hemorrhages. The peripheral zone was homogeneous, opaque and pale gray and contained irregular calcific deposits. The smaller nodule was similar. Microscopic examination revealed that the nodules were adenomas (fig. 4). In some areas, however, there were evidences of malignancy in the form of abnormal cell structure, hyperchromatosis, mitotic figures, irregularities of cell growth and invasion of blood vessels. The histologic diagnosis was carcinoma and adenoma of the thyroid gland.

Other laboratory data were essentially normal.

The patient made a satisfactory recovery from both operations, was discharged on May 29 and is now receiving roentgen therapy to her skull.

The final diagnosis was carcinoma and adenoma of the thyroid gland with metastases to the right frontal bone.

COMMENT

The first case falls very nicely into the category of "benign metastasizing goiter." Yet in spite of the benign histologic appearance of both the primary lesion and the secondary lesions, the condition is to be regarded as malignant. The presence of secondary deposits in the skull indicates that invasion through blood vessels had taken place at some time in the history of the primary thyroid neoplasm. This is prima facie evidence of malignancy. As has been noted, the histologic structure is of little importance in the determination of malignancy of thyroid tissue. It is also possible that serial sections of the thyroid gland might have uncovered a miniature area of carcinoma. Such examination was not feasible in this case because of technical difficulties. Several blocks were studied however.

The second case is illustrative of the fact that metastases from thyroid carcinoma may bear little or no resemblance to the primary lesion and that unless the primary tumor is also studied, the true nature of the condition remains unrecognized. Because of the clinically benign appearance of the thyroid gland and the benign histologic character of the cranial tumor, this case would undoubtedly have been recorded in the older literature as one of metastasizing thyroid adenoma. The tumor's pulsatile nature and the audible bruit are in keeping with the well recognized clinical features of these lesions.

SUMMARY AND CONCLUSIONS

The literature of so-called "benign metastasizing goiter" is briefly reviewed.

In spite of the histologically benign appearance of the primary tumor or the metastases or both, the condition is to be regarded as malignant.

Two cases illustrating the outstanding clinical and pathologic features of this condition are reported.

Intracranial neoplasms in patients with goiters should be considered metastatic until proved otherwise, even though the thyroid lesion appears to be insignificant.

Treatment consists of radical surgical removal of the primary and secondary lesions followed by roentgen therapy.

THE SOLID CARBON DIOXIDE–FERRIC CHLORIDE TECHNIC FOR HEMOSTASIS

EXPERIMENTAL STUDY OF ITS EFFECTIVENESS IN BRAIN, VISCERA AND SUPERIOR SAGITTAL SINUS

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NEW YORK

A new technic has been developed with experimental animals for the control of bleeding from the cross-sectional surfaces of vessels in the brain and the viscera, as encountered after excision of blocks of tissue, and from lacerations of the superior sagittal sinus. At this time this procedure may have special application in war surgery.

In a report on a new method of excising blocks of brain tissue with minimal bleeding by means of liquid nitrogen and a mechanical device, Koskoff and his associates [1] stated: "The slight hemorrhage which usually follows the removal of the instrument is easily controlled by pouring a small amount of liquid nitrogen into the bleeding area. This congeals the blood and a dry crater remains." In an earlier paper [2] I have discussed the effects of low temperature freezing on cerebral and vascular tissues. This type of refrigeration preserves cell structure; the tissues return to normal on thawing. Therefore, low temperature freezing can be expected to act only as a temporary hemostatic. In order to corroborate this theory, a block of tissue was excised from the brain of a cat and liquid nitrogen was applied to the oozing vessels in the crater. The area was frozen, and bleeding stopped. Within about thirty seconds, when thawing had taken place, bleeding began again. It appears, then, that freezing with liquid nitrogen or solid carbon dioxide can act only as a temporary hemostatic.

The possibility of utilizing refrigeration with liquid nitrogen or solid carbon dioxide as a preliminary to chemical coagulation for permanent hemostasis presented itself. Styptics alone are relatively ineffective, because they are readily diluted and washed away by flowing blood. Preliminary refrigeration stops blood flow temporarily, freezing the accumulated blood and the mouths of the vessels; a chemical coagulant might then be applied and bleeding be stopped permanently.

Liquid nitrogen and solid carbon dioxide were considered as freezing agents. Liquid nitrogen was both sprayed and poured on bleeding areas of brain and liver. It was found that bleeding of more than minimal degree prevented refrigeration, because the freezing liquid was washed away. On the other hand, blocks of solid carbon dioxide applied with moderate pressure were in all cases effective in freezing the bleeding area.

Various chemical coagulants were tested, including silver nitrate, tannic acid, zinc chloride, copper sulfate, aluminum sulfate, potassium aluminum sulfate, iron ammonium sulfate, and ferric chloride. Of these a 20 per cent solution of ferric

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1. Koskoff, Y. D.; Markson, V., and Wall, N. M.: Method for Removal of Areas of Brain Following Freezing in Situ, Am. J. Surg. **50**:271-273, 1940.

2. Ebin, J.: The Carbon Dioxide Snow-Electrocautery Technique for Occlusion of Large Veins: Suggested Application to Venous Angioma of the Brain, Surg., Gynec. & Obst. **76**:43-50, 1943.

chloride was found most effective. Ferric chloride combines with proteins, principally those of the plasma (albumin, globulin and fibrinogen), to form ferric proteinate, a black coagulum which occludes the mouths of the torn vessels.

Methods of handling and shaping the refrigerant have been previously presented.[2] It is a white solid having a temperature of —78 C. and may be kept in a vacuum jar, from which there is a loss of 5 per cent per day. The material is surrounded by a film of gas which acts as an insulator and must be removed by pressure before freezing can occur. Solid carbon dioxide is bacteriologically sterile. Blocks are cut with a hack saw. Smaller pieces are formed with a hammer and a moderately keen-edged knife. Narrow wedges are cut with a heated knife blade used with a sawing motion.

The refrigerant must come in contact with all bleeding points for coagulation to be fully effective. The solid carbon dioxide must therefore approximately fit the bleeding area; various shapes may be necessary. For flat surfaces, blocks of solid carbon dioxide are satisfactory. For craters, such as are seen after excision of blocks of cerebral tissue, rounded presenting surfaces are best. Such a surface is made by rounding off the sharp corners of a square presenting surface with the flat of a knife blade heated in a Bunsen flame. For use in lacerations, such as may occur in the liver, narrow wedges are most satisfactory, since they permit freezing of vessels in the deepest part of the tear. Various sizes and shapes of solid carbon dioxide are prepared before operation and kept in a vacuum jar until needed. A small sterile knife is kept on the instrument table to make minor changes in the shape of the solid carbon dioxide as required. An Allis clamp, or a large curved clamp with close-fitting rubber tubing on the prongs, is used to handle the refrigerant.

Ferric chloride is obtained in crystalline form, and a 20 per cent solution in distilled water is made up. The solution is then passed through filter paper. It has a p_H of 1 and is therefore bacteriologically sterile. Repeated efforts to grow organisms from it, with agar, blood agar, broth, blood broth and anaerobic meat broth as culture mediums have failed.

The ferric chloride solution is best applied by means of absorbent cotton. Johnson and Johnson absorbent cotton pellets, medium size, no. 2, are used, but any form of this material is satisfactory. Dental rolls are unsatisfactory as they do not readily give up the solution. A suction tip of large caliber is used.

The best results are obtained when the suggested technic is closely adhered to.

BRAIN

Various methods are now in use for the control of bleeding from the cross-sectional surfaces of blood vessels in the brain. Horsley[3] first suggested the application of small pieces of muscle to bleeding points. Cushing[4] introduced the silver clip and was the first to use the electrocautery[5] in neurosurgery. Dry absorbent cotton or absorbent cotton moistened in warm saline solution is also helpful. Frequently, however, these are not adequate, and hemorrhage becomes a serious problem.

3. Horsley, V.: Note on Hemostasis by Application of Living Tissue, Brit. M. J. **2**:8, 1914.

4. Cushing, H.: The Control of Bleeding in Operations for Brain Tumors, with the Description of Silver "Clips" for the Occlusion of Vessels Inaccessible to the Ligature, Ann. Surg. **54**:1-19, 1911.

5. Cushing, H., and Bovie, W. T.: Electrosurgery as Aid to Removal of Intracranial Tumors, Surg., Gynec. & Obst. **47**:751-784, 1928.

The solid carbon dioxide–ferric chloride technic has been used successfully for the control of bleeding in the brains of 12 cats and 4 dogs. Alexander and Putnam [6] have divided cerebral blood vessels into seven types according to caliber. Types 7, 6 and 5 include the internal carotid, the middle cerebral and the anastomosing pial vessels; types 4, 3, 2 and 1 comprehend all intracerebral branches, type 4 representing the penetrating vessels, types 3 and 2 representing the branches resulting from the next two subdivisions and type 1 representing the capillaries. These authors stated: "In spite of the great differences in size of the body and brain, the intracerebral blood vessels of fourth, third, second and first orders are of approximately similar size in the human being, the cat, the guinea pig and the pigeon." The caliber of intracerebral vessels in the experimental animal thus closely approximates the caliber of those in man. Bleeding from pial vessels, which are larger in the human being, may be controlled by silver clips.

The tissue removed from cats has on the average measured 1 cm. in diameter and 0.5 cm. in thickness; that from dogs, 2 cm. in diameter and 0.5 cm. in thickness. Pieces of solid carbon dioxide of approximately the same size with a rounded presenting surface have been used, the depth being greater than that of the excavation to allow room for grasping the material with a clamp. For larger areas, pieces with presenting surfaces 2.5, 3, 3.5 or 4 cm. in diameter may be used.

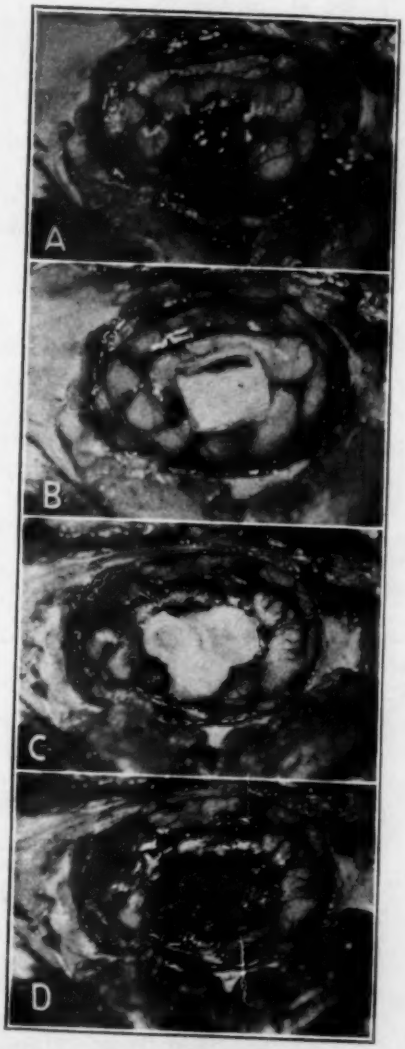
A wide exposure of brain is obtained, and the scalp, muscle, bone and dura are walled off with flat cotton strips in order to prevent contact with the ferric chloride solution. The removal of a block of tissue from the brain is followed by brisk bleeding. The solid carbon dioxide is applied with moderate pressure, care being taken that contact is made with all bleeding points. It sometimes requires manipulation of the refrigerant in order to touch and freeze all these points. While the refrigerant is in place, the pial vessels bordering on the area are clipped and cotton strips are placed on the adjacent cortex. After the area has been frozen for one minute the refrigerant is removed. The frozen area is seen to be covered with a white frost. Cotton pellets soaked in ferric chloride solution are then placed on the frozen part for one minute. At the end of this time the pellets are carefully taken off, and the excess solution is removed by suction. The treated area is seen to be covered with a black coagulum of ferric proteinate about 0.3 mm. in thickness (figure). If blood seeps through the ferric chloride pellets, the pellets are removed. The area is irrigated and suction is used in order to locate the bleeding points, and freezing and coagulation are repeated.

In most cases the technic has been successful on the first attempt. In a few experiments several repetitions have been required, but in every instance bleeding was stopped. The most frequent cause for the necessity of repetition has been failure to touch deep bleeding points with the refrigerant. A second cause, which stems from the difficulty of adequate exposure in relatively small animals, has been the occasional flow of blood from some source outside the excised area onto the frozen brain. This tends to dilute and wash away the ferric chloride solution.

Care must be exercised to avoid pushing the refrigerant into a ventricular cavity, since in this situation carbon dioxide gas is given off by the solid carbon dioxide and the cavity is expanded. This is particularly likely to happen in the brains of small animals, such as the cat, because the layer of tissue external to the ventricle is relatively thin. ***Therefore, if the bleeding area communicates with or is directly adjacent to a part of the ventricular system, the procedure is not used.***

6. Alexander, L., and Putnam, T. J.: Pathological Alterations of Cerebral Vascular Patterns, A. Research Nerv. & Ment. Dis., Proc. (1937) **18**:471-543, 1938

In a previous report [2] the effects of low temperature freezing on brain tissue were considered in detail. The conclusions reached were that low temperature freezing in itself does not injure tissue, that the damage following refrigeration with solid carbon dioxide is the result of pressure and that this damage is superficial and negligible. The effects of ferric chloride alone and of solid carbon dioxide and ferric chloride on cortical and subcortical tissue were studied. Two cats were treated with cotton pellets soaked in a 20 per cent solution of ferric



Bleeding from a crater in the brain of a cat stopped by the use of solid carbon dioxide and ferric chloride (× 1): *A*, bleeding; *B*, frozen; *C*, ferric chloride pellets in place; *D*, crater covered with coagulum and bleeding stopped.

chloride applied to an area of cortex 1 cm. in diameter for one minute. When the pellets were removed a pale tan discoloration was visible in the treated area. The surrounding brain tissue was normal in appearance. The cats were normal during a period of three weeks, at the end of which they were killed. At autopsy the same pale tan discoloration was noted. There was no evidence of infection or sterile reaction. Cross section revealed no injury. Microscopic examination

showed absence of the pia-arachnoid in parts of the treated area and occasional small areas of fibrosis in the zonal layer of the cortex.

A piece of solid carbon dioxide 1 cm. in diameter was applied with moderate pressure to an area of cortex in each of 2 cats for one minute, and then cotton pellets soaked in a 20 per cent solution of ferric chloride were placed on the same area for the same length of time. On removal a pale tan discoloration was seen. No abnormality could be detected in the behavior of the animals during the postoperative period of three weeks, at the end of which they were killed. Autopsy disclosed no evidence of infection or sterile reaction. On cross section there was no gross evidence of damage. Microscopic examination in 1 case disclosed normal gray and white matter except for a minute area 1 mm. wide and 0.6 mm. deep in one section. In this area cortical tissue was replaced by fibroblasts, lymphocytes and fat granule cells. In the second specimen a similar picture was seen.

Pieces of tissue were removed from the brains of 2 dogs. Bleeding was stopped by means of solid carbon dioxide and ferric chloride. The animals were normal throughout the postoperative period. At the end of three weeks they were killed. Bleeding had not recurred, and there was no evidence of infection or sterile reaction. Cross section revealed that the excised area had been replaced by fibrous tissue. Surrounding tissues were of normal appearance. Microscopic examination in both cases showed fibrous tissue, lymphocytes and fat granule cells in the area of excision. Adjacent nerve tissue was normal.

The procedure described has been effective in stopping bleeding from the cross-sectional surfaces of vessels in the brains of experimental animals. There has been no recurrence of bleeding, and the damage done by the procedure has been insignificant. This technic may be similarly effective in the control of bleeding from nerve and tumor tissue in the brain of the human being.

VISCERA

Bleeding from the liver may occur in the course of a surgical procedure, such as resection for removal of neoplasm, or as the result of trauma. Traumatic lesions are of two types. In the first the abdominal wall is intact, injury being the result of a contusing force. From this type of injury several varieties of damage to the liver may result. There may be lacerations, most frequently sagittal, affecting the convex surface and extending for a varying distance into the depth of the organ; the right lobe is more commonly affected. There may be a subcapsular hematoma without laceration of the capsule, or there may be damage in the depths of the organ with the formation of a central hematoma. In the second type of trauma to the liver lesions are produced by cutting instruments which tear through the abdominal wall. Such lacerations are usually the result of stab wounds and injuries due to firearms.

The generally favored methods of controlling bleeding from the liver are suture and tamponade. Mattress sutures of thick catgut on round blunt needles are favored. Suture with catgut soaked in tissue extracts has also been reported by Dainelli.[7] The friability of the tissues of the liver tends to make this method of controlling bleeding from the liver ineffective. Packing with gauze is on the whole the most reliable method; the gauze may first be soaked in a hemostatic solution. The tampon is left in place for from two to twelve days. Infection and recurrence of hemorrhage on removal of the packing are not infrequent. Additional methods of hemostasis include the use of heated air, water vapor, the actual cautery, omentum, fat, muscle, bone powder, tissue extracts, epinephrine

7. Dainelli, M.: Ricerche sperimentali sull'use di estratti di tessuti a scopo emostatico, Ann. ital. di chir. **13**:989-1032, 1934.

and gelatin. Marcucci [8] and Cué [9] have reported on the experimental use of a gum, tragacanth.

Shedden and Johnston [10] reported a case of traumatic laceration of the liver in which bleeding was controlled by gauze packing. In Christopher's [11] case bleeding from the liver was controlled by gauze packing, which was removed on the eighth postoperative day. Removal of the gauze was followed by the development of a subphrenic abscess which required rib resection for drainage. The patient had two episodes of acute intestinal obstruction which required laparotomies with prophylactic enterostomies. Branch [12] and Pickworth [13] were able to control bleeding from traumatic lacerations of the liver by use of mattress sutures.

The solid carbon dioxide–ferric chloride technic has been used successfully in lacerations of the liver in 12 cats and 2 dogs. Bleeding from lacerations in this organ arises from large branches of the hepatic artery, the hepatic vein and the portal vein and from the small vessels of the parenchyma. In these experiments bleeding from all vessels has been stopped. The large vascular trunks are naturally of greater size in the human being. Bleeding from these vessels might be controlled by use of clamp and ligature.

The procedure has been used on areas of the liver from which a section of the surface has been removed and on lacerations extending into its depth. For surface wounds blocks of solid carbon dioxide of approximate size are satisfactory. For lacerations wedges of the refrigerant have been found more effective, since their shape permits contact between the dry ice and the deepest bleeding points. The incisions have been 4 cm. in length, with a greatest depth of 0.8 cm. Wedges used have been of a length and depth greater than that of the laceration to assure contact between the refrigerant and bleeding tissue throughout the entire extent of the tear and to allow room for grasping the material with a clamp. Those used in these experiments have been 5 cm. long, 2.5 cm. thick and 1 cm. wide, the angle of the sides being approximately 22 degrees. Larger wedges may be used for larger lesions. Where slight changes are necessary to make the shape of the refrigerant conform to that of the lesion, they may be made with a knife. In bleeding areas of different form, such as might result from the excision of a block of tissue, a piece of solid carbon dioxide of approximately the same shape may be molded in the manner described previously for use in operation on the brain.

As an example, the procedure in the case of a laceration may be considered. To expose the liver a right pararectus upper abdominal incision is made. The sides of the wound are walled off with gauze to prevent contact with the dry ice or the ferric chloride solution. An incision is made in the liver with a scalpel. A wedge of solid carbon dioxide is inserted into the laceration, and moderate pressure is applied. At the same time the sides of the tear are compressed manually against the refrigerant either from behind or laterally. Manipulation of the refrigerant is sometimes required in order to freeze all bleeding points. While the refrigerant is in place flat cotton strips are placed on the adjacent liver tissue. After the bleeding surfaces have been frozen for one minute, the refrigerant is removed. The frozen area is seen to be covered with a white frost. Absorbent cotton pellets

8. Marcucci, G.: L'emostasi epatica: Ricerche sperimentali, Arch. ital. di chir. **50**:101-119, 1939.

9. Cué, V. B.: Hemostasia hepática: El tuffon, Rev. méd. de Rosario **31**:148-152, 1941.

10. Shedden, W., and Johnston, F.: Traumatic Rupture of Liver, New England J. Med. **213**:960-965, 1935.

11. Christopher, F.: Rupture of Liver, Ann. Surg. **103**:461-464, 1936.

12. Branch, C. D.: Injury of Liver: Report of Two Cases, Ann. Surg. **107**:475-477, 1938.

13. Pickworth, M. E.: Traumatic Rupture of Liver: Report of Case, California & West. Med. **51**:328-329, 1939.

soaked in ferric chloride solution are then placed on the frozen part for one minute. At the end of this time the pellets are carefully taken off and the excess solution is removed. The treated area is seen to be covered with a black coagulum of ferric proteinate. If blood seeps through the pellets they are removed and the entire procedure is repeated. Often the procedure had to be repeated several times in order to stop all bleeding, but in every case the flow of blood was stopped. It has not been necessary in these experiments to clamp and ligate any of the large vascular trunks.

The effects of the application of dry ice and ferric chloride to hepatic tissue were studied in long term experiments. With each of 3 cats a piece of solid carbon dioxide 1 cm. square was applied with moderate pressure to the liver for one minute. On removal of the refrigerant a white frost was seen on the frozen surface, which thawed after about one minute. A dark red discoloration was then noted at the site of freezing. The animals were entirely normal during the postoperative period. At the end of three weeks autopsy revealed no evidence of infection or sterile reaction in the liver or the abdominal cavity. A gray discoloration was seen on the surface of the area which had been frozen. On section this discoloration was apparent to a depth of 1.5 mm. Microscopic examination showed that in the discolored area hepatic tissue had been replaced by fibrous tissue, lymphocytes, blood pigment and fat cells. Surrounding tissue was normal. The mildness of damage conforms with the results of low temperature freezing of brain tissue.

Cotton pellets soaked in ferric chloride solution were applied to the livers of 3 cats for one minute. On their removal a gray discoloration was seen over the treated area. The animals were normal during the postoperative period. Autopsy at the end of three weeks showed no evidence of infection or sterile reaction in the liver or abdominal cavity, nor were there any adhesions. On section through the treated area there was no gross evidence of damage. Microscopic examination revealed detachment of the capsule of the liver in the areas treated. All other structures were normal.

Incisions were made in the livers of 3 cats. Bleeding was stopped by the use of solid carbon dioxide and ferric chloride. During the postoperative period the animals were normal. Autopsy three weeks later showed that there had been no recurrence of bleeding, nor was there evidence of infection or sterile reaction in the liver or abdominal cavity. The only adhesion noted had formed between the treated site and the anterior abdominal wall in 1 animal which had been well and active during the postoperative period. All specimens showed a gray discoloration over the treated surface. On section the line of incision was seen to be occupied by fibrous tissue. On microscopic examination fibrous tissue and collections of lymphocytes were seen in this area. Surrounding tissue was normal.

The solid carbon dioxide–ferric chloride procedure has also been successful in controlling bleeding from lacerations of the lung in cats, and from the spleen and the kidney in both cats and dogs.

Through use of this technic bleeding in the viscera of experimental animals has been stopped. There has been no recurrence of bleeding, and the damage done by the procedure has been negligible. This method of hemostasis may be successful in controlling parenchymatous bleeding from the liver, as well as the lung, the spleen, the kidney, the thyroid and the pancreas in the human being.

SUPERIOR SAGITTAL SINUS

Lacerations of the superior sagittal sinus may occur in the course of an operative procedure or as the result of a depressed fracture of the vault of the skull near the midline. The sinus walls contain no elastic tissue and are held rigidly open by

the pull of the dura mater. For this reason bleeding from a torn superior sagittal sinus may be very severe. In lacerations resulting from depressed fractures bleeding may occur immediately or the bone fragment may plug the opening. However, hemorrhage does occur when the fragment of bone is elevated at operation. Loss of blood in these cases may be severe and even fatal.

Methods now in use for the control of bleeding from the superior sagittal sinus include application of slabs of muscle to the tear, packing with gauze, passage of ligatures around the sinus, suture of the tear and application of hemostatic clamps. Slabs of muscle may be successfully used for small wounds but are not effective in larger lacerations even when held in place with dural sutures running across the sinus. Gauze packing is not always adequate for control of bleeding from large tears. Furthermore, when the gauze is removed there is always the danger of recurrence of hemorrhage. Passage of ligatures involves the danger of lacerating the underlying brain, nor is it always successful, since the triangular shape and rigid walls of the sinus resist occlusion by ligature. Suture of the tear with fine silk is difficult in the presence of bleeding. The removal of hemostatic clamps may be accompanied by severe hemorrhage.

Bailey [14] reported a case in which a small tear was controlled with a piece of muscle. In Chavanne's [15] case hemorrhage was arrested by a tampon left in place for six days. Removal was accomplished without bleeding. Bleeding from the superior sagittal sinus was stopped by Bagley [16] with gauze packing. Carlucci [17] encountered severe bleeding which packing did not stop. Suture-ligatures about the sinus anterior and posterior to the tear finally arrested the hemorrhage.

The solid carbon dioxide–ferric chloride procedure has been used successfully in lacerations of the superior sagittal sinus in 5 dogs. In each case a coagulum of ferric proteinate formed over the tear and bleeding stopped. These sinuses measured from 0.3 to 0.35 cm. at their widest point, as compared with about 1 cm. in man.

The principle underlying this procedure is much the same as that described for elimination of cross-sectional bleeding in the brain and in the liver. The flow of blood is temporarily stopped by freezing the torn sinus and the entering superior cerebral veins on each side. The ferric chloride solution may then act on the lacerated surface without being diluted or washed away.

A wide exposure of the sinus is obtained, after which it is torn for its entire width with a no. 11 Bard-Parker blade. A block of solid carbon dioxide 4 cm. long, 4 cm. thick and 2 cm. wide is then applied with moderate pressure to the bleeding sinus. A similar piece is then placed on each side of it in order to freeze the entering superior cerebral veins. While the refrigerant is in place the surrounding scalp, muscle, bone and dura are walled off with gauze and cotton strips. After one and a half minutes the refrigerant is removed, and absorbent cotton pellets soaked in 20 per cent ferric chloride solution are applied to the area of laceration. At the end of one and one-half minutes these are removed. The treated area is seen to be covered with a black coagulum of ferric proteinate. If bleeding recurs while the cotton pellets are in place they are removed and the procedure is repeated. In 3 cases the technic was successful on the first attempt, and in the remaining 2 cases several repetitions were necessary. No convulsions were noted during freezing,

14. Bailey, P.: Wounds of Superior Longitudinal Sinus, S. Clin. North America **9**:395-405, 1929.

15. Chavanne, F.: Hémorragie du sinus longitudinal supérieur, Oto-rhino-laryng. internat. **16**:231-232, 1932.

16. Bagley, C., Jr.: Traumatic Longitudinal Sinus Lesions: Report of Two Cases, Surg., Gynec. & Obst. **58**:498-502, 1934.

17. Carlucci, G. A.: Injury to Longitudinal Sinus Accompanying Depressed Fracture of Skull, Am. J. Surg. **45**:120-124, 1939.

but in 2 animals occasional temporary apnea for from ten to fifteen seconds was observed while the dry ice was in place. In each case respirations returned to normal.

Two of these animals were allowed to live for three weeks. After the first few days they were alert and active. They showed no symptoms or signs of cerebral damage. At autopsy there was no evidence of recurrence of bleeding or of infection or sterile reaction. In one specimen the sinus was occluded by fibroblasts; in the other, blood pigment was seen. The cortex of the most medial gyrus on each side was replaced by fibrous tissue and fat granule cells to a depth of 1.5 mm. Tissue below that was normal. In the human cortex, whose greatest depth is 4 mm. in the motor area, such damage should in most instances be negligible.

The solid carbon dioxide–ferric chloride procedure has been successful in stopping bleeding from lacerations of the superior sagittal sinus in dogs. Bleeding has not recurred, and damage has been slight. The technic may perhaps be effective in controlling bleeding from lacerations of the superior sagittal sinus in the human being.

SUMMARY

A technic for the control of bleeding from the cross-sectional surfaces of vessels in the brain and the viscera and from lacerations of the superior sagittal sinus has been developed with experimental animals. This procedure may be effective in similar situations in human beings and may be of value in war surgery.

Dr. Tracy J. Putnam, in whose laboratory this work was done, gave aid and encouragement.

TREATMENT OF ACUTE ARTERIAL OCCLUSION BY MEANS OF INTERMITTENT VENOUS OCCLUSION

REPORT OF A CASE

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BOSTON

Ligation of a main artery of the lower extremity, such as the common iliac, external iliac or common femoral, may result in gangrene even in the presence of a normal arterial system. A number of methods are available to prevent such a catastrophe from occurring. Therapeutic venous occlusion, produced by ligation of the concomitant vein when it is necessary to ligate a major artery, is one of the methods which has been advocated. This method was propounded by Makins,[1] a British surgeon during World War I. He collected a series of cases to show that this procedure reduced the incidence of gangrene when it was necessary to ligate a major artery to a limb. Numerous attempts in the laboratory have been made to explain this somewhat paradoxic phenomenon. Some investigators [2] have produced experimental evidence to prove that the actual arterial inflow to an extremity is increased after this procedure, while others [3] have presented evidence that it is decreased. One of the most recent articles on the subject was published by my coworkers and me.[4] We showed that an actual increase in the arterial inflow to a dog's hind extremity occurred after occlusion of the iliac vein both with the arterial system intact and when the femoral artery had been occluded (figs. 1 and 2). The Rein thermostromuhr method of measuring blood flow,[5] which measures cubic centimeters of blood per minute flowing through a given blood vessel, was used. It was also demonstrated that the actual increase in arterial blood flow took place during the period of venous occlusion and not after the release of it. Collens and Wilensky [6] in 1936 reported the use of a pneumatic tourniquet to produce

From the Surgical Service of the Massachusetts General Hospital.

1. Makins, G. H.: (*a*) Hunterian Oration, 1917, on the Influence Exerted by the Military Experience of John Hunter on Himself and on the Military Surgeons of Today, Lancet **1**:249, 1917; (*b*) Gunshot Injuries to the Blood-Vessels, New York, William Wood & Company, 1919.

2. Holman, E.: (*a*) Surgery of Large Arteries, Ann. Surg. **85**:173, 1927. (*b*) Holman, E., and Edwards, M. E.: A New Principle in the Surgery of the Large Arteries, J. A. M. A. **88**:909 (March 19) 1927. Pearse, H. E.: A New Explanation of the Improved Results Following Ligation of Both Artery and Vein, Ann. Surg. **86**:850, 1927. Theis, F. V.: Ligation of Artery and Concomitant Vein in Operations on Large Blood Vessels, Arch. Surg. **17**:244 (Aug.) 1928.

3. Brooks, B., and Martin, K. H.: Simultaneous Ligation of Vein and Artery, J. A. M. A. **80**:1678 (June 9) 1923. Brooks, B.: Surgical Applications of Therapeutic Venous Obstruction. Arch. Surg. **19**:1 (July) 1929. Montgomery, M. L.: Therapeutic Venous Occlusion, ibid. **24**:1016 (June) 1932.

4. Linton, R. R.; Morrison, P. J.; Ulfelder, H., and Libby, A. L.: Therapeutic Venous Occlusion, Am. Heart J. **21**:721, 1941.

5. Rein, H.: Die Thermostromuhr. Ein Verfahren zur fortlaufenden Messung der mittleren absoluten Durchflussmengen in uneröffneten Gefassen in situ, Ztschr. f. Biol. **87**:394, 1928. Herrick, J. F., and Baldes, E. J.: Thermostromuhr Method of Measuring Blood Flow, Physics **1**:407, 1931.

6. Collens, W. S., and Wilensky, N. D.: (*a*) Intermittent Venous Occlusion in Treatment of Peripheral Vascular Disease, J. A. M. A. **109**:2125 (Dec. 25) 1937; (*b*) The Use of Intermittant Venous Compression in Treatment of Peripheral Vascular Disease, Am. Heart J. **11**:705, 1936.

intermittent venous occlusion in the treatment of chronic obliterative arterial disease. A pressure in the tourniquet at or slightly below diastolic blood pressure was recommended. The effect of this method of venous occlusion on the arterial inflow to a dog's extremity was studied also with the Rein thermostromuhr, and an increase was observed during the period of occlusion similar to that produced by venous ligation (fig. 3).

The purpose of this paper is to present a case in which acute arterial occlusion of the ipsilateral external iliac and hypogastric arteries in a woman aged 58 years was treated with intermittent venous occlusion. Gangrene of the extremity was prevented despite the absence of all arterial pulsations in the leg. The patient was discharged from the hospital three weeks after the arterial occlusion, at which

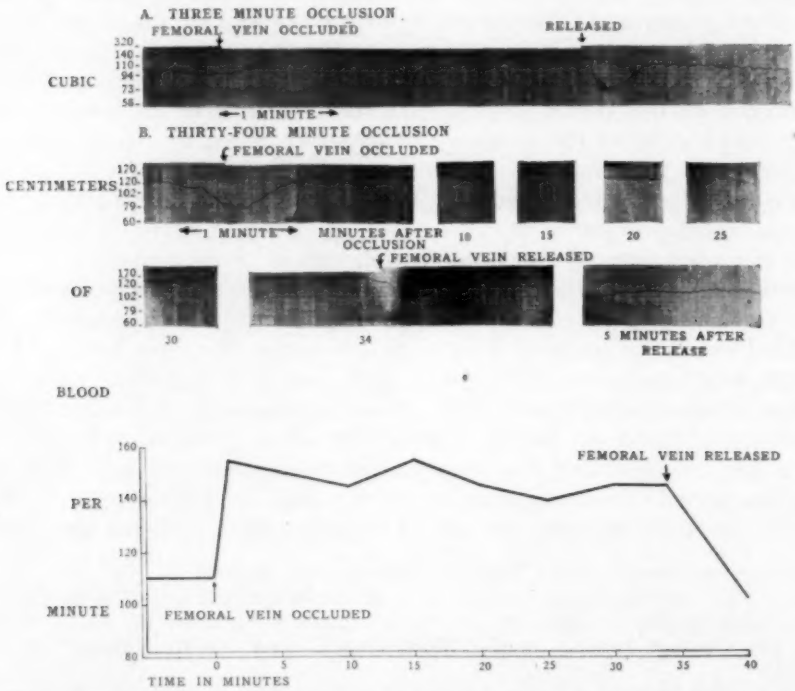

Fig. 1.—The effect of venous occlusion in the ipsilateral limb on the normal arterial blood flow to an extremity (sodium amytal anesthesia). Note the rapid increase in the flow of blood in the femoral artery after occlusion of the femoral vein in the three minute occlusion record, namely from 100 cc. per minute to 230 cc. per minute. In the thirty-four minute record, the increase is from 110 cc. per minute to 155 cc. per minute. It is also to be noted that the blood flow persisted at 145 cc. per minute until the femoral vein was released. This shows that the increase in arterial blood flow is concomitant with the venous occlusion. Figures 1, 2 and 3 have been previously published (Linton and others [4]).

time she was able to walk about the hospital. Two years and three months later, at the time of this report, she was able to walk without discomfort.

REPORT OF CASE

A 58 year old white native American woman was first admitted to the Baker Memorial Hospital Jan. 29, 1940 with a five months' history of slowly increasing abdominal distention, weakness and loss of weight. Associated with these symptoms she had had frequent attacks of crampy abdominal pain and some intermittent severe pain in the left costophrenic angle. The menopause had occurred in 1932, but in the eight or nine months preceding admission

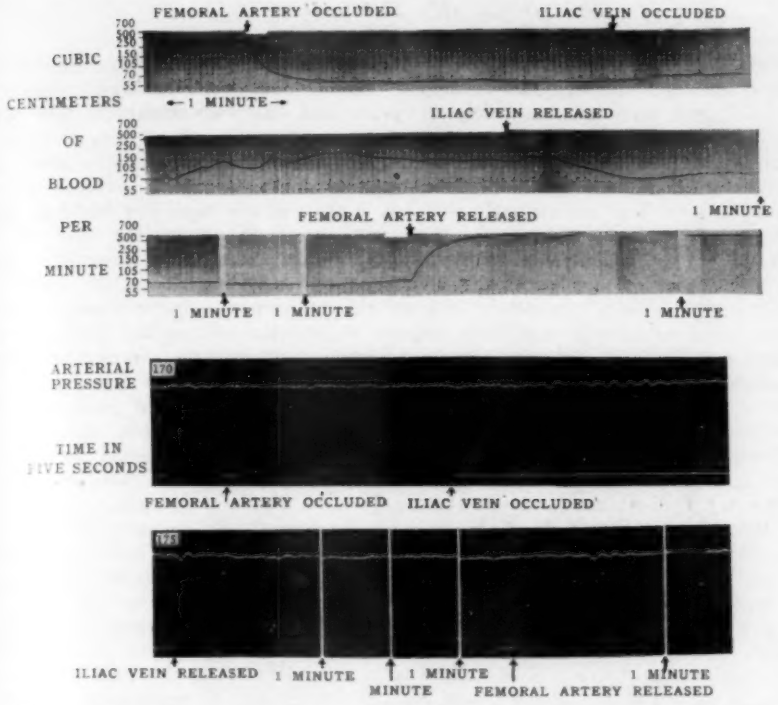

Fig. 2.—The effect of venous occlusion on the flow of blood in the iliac artery in the presence of acute arterial insufficiency (sodium amytal anesthesia). After occlusion of the femoral artery, note the decrease in arterial blood flow from 450 cc. a minute to 60 cc. a minute and the increase in blood flow to 140 or 150 cc. a minute after occlusion of the iliac vein. It will be seen that this increase persisted as long as the occlusion was present and that after the release of the iliac vein the flow returned to the preocclusion level. This experiment had no effect on the blood pressure of the animal.

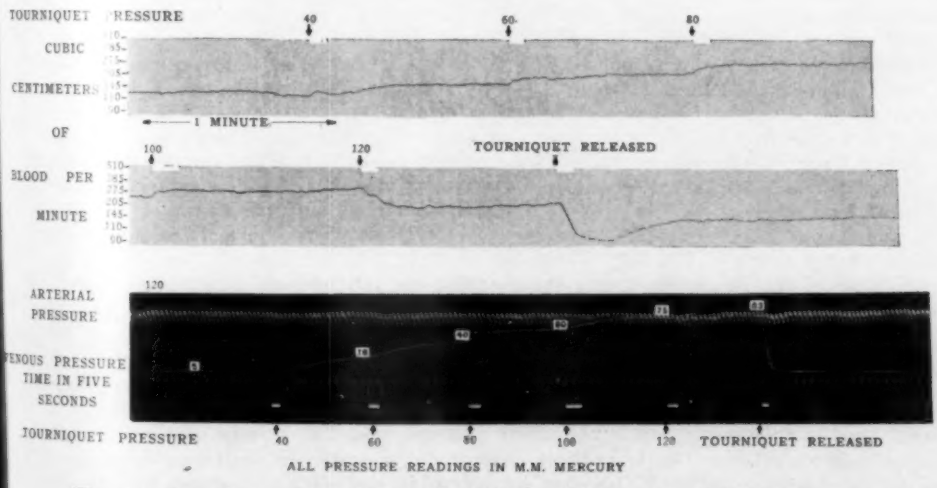

Fig. 3.—The effect on the flow of blood in the iliac artery of increasing venous pressures by means of a pneumatic tourniquet applied to the thigh. It is to be noted in this record that with each increase in the venous pressure of the extremity by raising the pressure in the tourniquet there was an increase in the arterial blood flow until the venous pressure reached a level above 75 mm. of mercury. It will be seen that the venous pressure can be elevated much higher by this means than by ligation of the main vein of an extremity. The blood flow was increased by this means from 115 cc. a minute to 280 cc. a minute, whereas obstruction of the iliac vein in the same animal produced a rise from 115 cc. a minute to only 215 cc. a minute.

to the hospital she had had a slight amount of vaginal bleeding at intervals. In the last month severe orthopnea and dyspnea had developed. She required many pillows in order to sleep at night. She had been married thirty-six years and had two daughters who were living and well.

Physical examination revealed an emaciated elderly woman sitting in a chair. When she lay down she became extremely dyspneic. The heart beat was irregular, with numerous extrasystoles, and the apex beat was palpable well out in the axillary line. The blood pressure was 156 systolic and 82 diastolic. There was complete flatness throughout the right side of the chest with a shift of the mediastinum to the left. Abdominal examination revealed a hard, irregular mass filling the lower part of the abdomen and extending above the umbilicus. It appeared fixed at the brim of the pelvis. Sounds due to peristalsis were unusually loud, but there did not seem to be any significant degree of intestinal distention. There was a small amount of free fluid in the abdomen. Pelvic examination showed the uterus to be small. The pelvic examination indicated that the mass arose in the region of the left ovary with some infiltration of the broad ligament. A note was made at this time that because of the possibility of infiltration it was thought that the tumor might be inoperable. Examination of the lower extremities revealed pitting edema of both ankles. There was good pulsation in the dorsalis pedis and the posterior tibial artery of both feet. A diagnosis of carcinoma of the left ovary, right-sided hydrothorax and extrasystoles of the heart was made. A roentgen examination of the chest confirmed the diagnosis of hydrothorax. On January 30, 2,700 cc. of reddish wine-colored fluid was removed from the right pleural cavity. Microscopic examination of this fluid revealed that it contained 35,700 red blood cells and 16,800 white blood cells per cubic millimeter and 16.7 Gm. of hemoglobin per hundred cubic centimeters. The differential blood smear showed 76 per cent polymorphonuclear cells, 12 small lymphocytes, 8 monocytes and 4 eosinophils. The red blood cells appeared normal, and the platelets were slightly increased. A roentgenogram of the chest after the removal of the fluid revealed a round, thick mass in the central pulmonary field opposite the eighth rib posteriorly, and there were also a number of smaller masses at the base of the left lung behind the heart shadow and a large sharply defined mass in the lower mediastinum.

In view of these findings it was considered that the patient had metastatic disease involving the lungs, farther advanced on the right side. Accordingly she was given a series of roentgen treatments and was discharged from the hospital on March 3. She refused operation at this time because she was greatly improved so far as her general condition and dyspnea were concerned.

She was readmitted to the hospital on April 10, in much the same condition in which she had been discharged except that the fluid in the right side of the chest had reaccumulated. The blood pressure was 185 systolic and 95 diastolic. A thoracentesis was performed and yielded 2,880 cc. of straw-colored fluid. The red cell count was 560 and the white cell count 6 per cubic millimeter of fluid. A laparotomy was performed on April 16 and a large solid carcinoma of the left ovary, measuring 23 cm. in diameter, was removed. The removal of the tumor was difficult because it was closely adherent to the left side of the pelvis. The left ureter passed through the mass, so that it was necessary to sacrifice it and remove the kidney. Damage to the hypogastric artery during the removal of the tumor made ligation necessary. The sigmoid loop of the colon was closely adherent to the growth and had to be dissected from it, and it was necessary to sacrifice the superior hemorrhoidal artery because it was involved in the tumor mass.

At the time of the operation it was thought that the left external iliac artery had not been damaged, but later developments proved this not to be the case. It probably was not ligated but was so severely traumatized that it became thrombosed. The patient was seen within two hours after the operation, at which time she was fairly well oriented and complained that her left foot was numb and cold and that she could not move it. Examination at this time revealed that the left leg was absolutely pulseless; even a femoral pulsation in the groin could not be made out. The blood pressure was 140 systolic and 80 diastolic. Intermittent venous occlusion was immediately commenced, a pneumatic tourniquet being placed as high on the thigh as possible. This was inflated to 50 mm. of mercury and left for nine minutes. At the end of this time the toes assumed a definite pink color. The pneumatic tourniquet was then released for one minute, and the leg immediately blanched. Intermittent venous occlusion was continued for the next forty-eight hours without interruption, with a cycle of nine minutes on and one minute off. During this period there was a gradual improvement in the circulation of the extremity, so that at the end of forty-eight hours it was possible to change the cycle to four minutes on and two minutes off. On April 26, the tenth postoperative day, intermittent venous occlusion was omitted all night because the patient was complaining of pressure on the thigh from the tourniquet and because considerable

edema of the left ankle had developed. The following morning the foot was warm, dry and pink. Subsequently the intermittent venous occlusion was used two hours on and one hour off during the day, with a cycle of three minutes on and three minutes off. On April 30, fourteen days after the operation, treatment was discontinued. The abdominal wound healed per primam intentionem. The patient was allowed out of bed on the fifteenth postoperative day and was discharged on May 3, the seventeenth postoperative day, at which time she was walking about the hospital.

Since her discharge from the hospital she has been examined a number of times. Her chief complaint has been of pain in the back. Roentgen examination revealed a destructive process involving the bodies of the thoracic portion of the spine. This lesion responded well to roentgen therapy, and on July 16, 1942 her condition had greatly improved. Her left leg still has no pulsations in it, and there are only slight oscillations in the thigh. When she has been standing all day there is a tendency toward edema, but this is controlled well with

Fig. 4.—A photograph of the patient's legs taken two years and three months after occlusion of the left external iliac artery and the hypogastric artery. Note that the left leg is normal in appearance compared with the right one except for slight swelling. There is no evidence that any of the toes had been gangrenous. No pulsations or oscillations were demonstrable at this time. Nevertheless the patient was able to walk a considerable distance without pain.

an elastic stocking (fig. 4). She is able to walk a distance of about a mile without pain, although not without some fatigue.

COMMENT

This case is of interest because it shows the value of the proper use of intermittent venous occlusion in the treatment of a case of acute major arterial occlusion. There can be little question that the arterial circulation to this patient's leg was seriously impaired. It is believed that without treatment gangrene of the foot and lower part of the leg would have developed.

Examination of the arterial system (fig. 5) indicates how meager the collateral arterial supply to the extremity was in this case. Blood could get to the extremity only via the direct anastomoses between the femoral artery and the epigastric and the deep circumflex iliac artery and indirectly through the branches of the hypogastric artery via the anastomoses with the ovarian, uterine, pubic and pudendal arteries of the same and the opposite side of the body. Nevertheless it was possible by means of intermittent venous occlusion to preserve the extremity and give the patient a useful leg.

It should be pointed out that ligation of the hypogastric artery and occlusion of the external iliac artery constitute a more serious arterial lesion than ligation

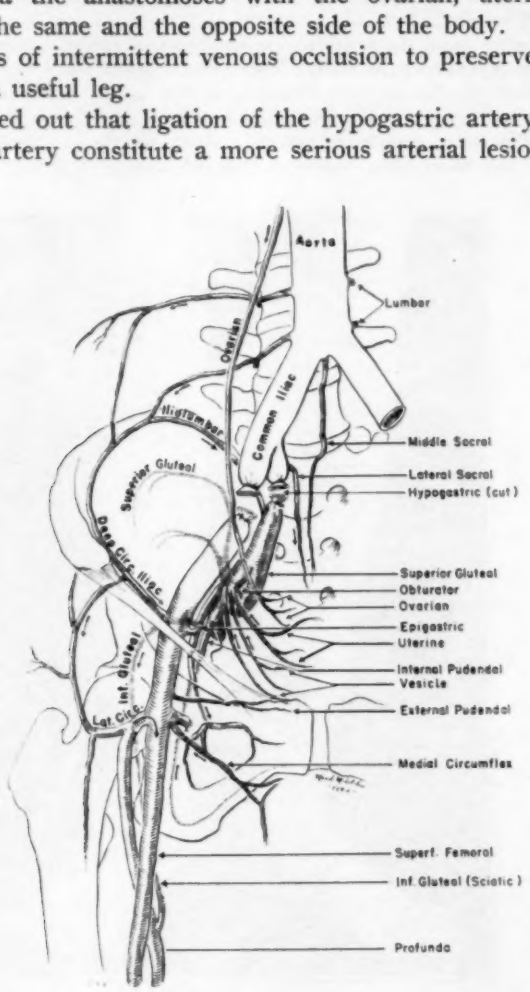

Fig. 5.—An anatomic drawing showing the collateral arterial circulation to the leg after division of the external iliac and the hypogastric artery. This lesion is comparable to the one described in this article. The chief collateral blood supply to the leg after such a vascular occlusion is from the lumbar arteries and epigastric arteries of the same side. The blood from the former reaches the femoral artery through anastomosis with the deep circumflex iliac artery, while the latter connects directly with it. A small amount of blood also reaches the extremity indirectly through obturator and inferior gluteal arteries, branches of the hypogastric artery from anastomoses of the ovarian, uterine, internal pudendal, external pudendal and medial circumflex arteries with the corresponding arteries of the opposite side of the body. It is obvious that the amount of blood reaching the leg through these channels must be greatly reduced from the normal, yet in spite of this it was possible with intermittent venous occlusion to prevent gangrene and save the extremity.

of the common iliac artery above its bifurcation (fig. 6). The reason is that when the common iliac artery is ligated any arterial blood entering the hypogastric artery through its collateral channels will be able to reach the extremity through the

external iliac artery, which of course is impossible if both arteries are occluded, as occurred in this case. Further evidence to substantiate this view is the statement made by Halsted[7]: "Ligation of the common iliac (artery) less endangers the vitality of the lower extremity, and makes easier the establishment of collateral circulation than does ligation of the peripheral vessels, for example, the external iliac (artery)."

The surgical removal of the large tumor was undertaken only with the patient's realization that her condition was critical and also that removal might not be possible. The surgical procedure that was carried out is perhaps open to some criticism, chiefly because of the lack of full realization of the damage to the external

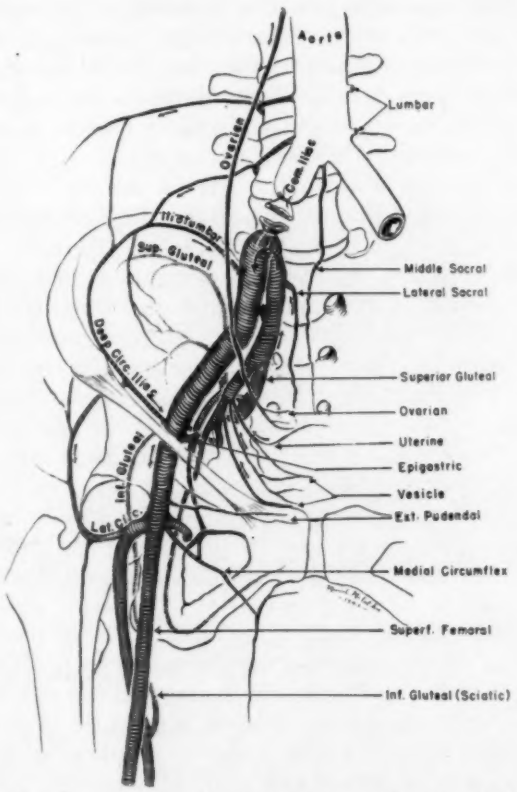

Fig. 6.—An anatomic drawing showing the collateral arterial circulation to the leg after division of the common iliac artery. Note that the blood which enters the hypogastric artery through its collateral channels can readily pass distally through the external iliac artery. Division of the common iliac artery, therefore, will not endanger the vitality of the extremity to the same extent as the lesion shown in figure 5.

iliac artery and the failure to ligate the common iliac vein. Furthermore, if a similar situation should arise again the importance of removing the lumbar ganglions on the left side would be recognized. Under the circumstances in this case removal could readily have been accomplished, since the ganglions were almost completely exposed when nephrectomy was done. These omissions are recognized, and the purpose in presenting the case is to show the value of intermittent venous occlusion in what seemed almost to be a hopeless situation.

7. Halsted, W. S.: The Effect of Ligation of the Common Iliac Artery on the Circulation and Function of the Lower Extremity, Bull. Johns Hopkins Hosp. **23**:191, 1912.

The technic of intermittent venous occlusion used in this case needs emphasis. The pneumatic tourniquet was applied as high as possible on the thigh, and the leg was elevated to the level of the heart, so that during the period of release of the venous occlusion the blood would readily empty from the veins of the leg. The pressure in the pneumatic tourniquet was maintained at 50 mm. of mercury. The cycle used for the first forty-eight hours was nine minutes of occlusion followed by one minute of release. The long period of occlusion in relation to the short period of release is considered highly important in the proper use of the intermittent venous occlusion. Thus in this case after inflating the tourniquet it was possible to see the gradual return of color to the extremity from above downward. Nine minutes was required for it to reach the ends of the toes, and as soon as the pressure in the venous tourniquet was released the leg, foot and toes blanched quickly. These observations corroborate the laboratory observations that it is during the period of venous occlusion that the arterial blood flow is augmented and that after release of pressure the flow decreases. As the collateral circulation gradually improved it was possible to change the cycle to one of four minutes of occlusion with two minutes of release.

Success in the treatment of major arterial occlusion by this method depends on several factors. First, and most important, the treatment should be commenced as soon as possible after the occurrence of the arterial occlusion. In the case reported intermittent venous occlusion was begun within two hours. If a period of eight hours or longer is allowed to elapse, intravascular thrombosis may occur in the distal part of the extremity and will preclude any chance to save the limb. Second, the extremity should be placed at the level of the heart, so that when the pressure in the tourniquet is released the blood and lymph will drain from the limb. The use of shock position if necessary for the general treatment of the patient is no contraindication to the use of intermittent venous occlusion, but allowance must be made in the timing of the cycle, since with the patient in this position blood will enter the extremity more slowly and drain out of it with greater rapidity. If it is necessary to keep the head much higher than the extremities, for instance in a patient with cardiac disease, intermittent venous occlusion should not be used, because the resulting venous and lymphatic stasis will produce edema and interference with the capillary circulation. Third, the pneumatic tourniquet should be placed as far proximal on the extremity as possible in order to include as much as possible of the collateral circulation. In the case reported it was placed on the thigh just distal to the groin. Fourth, a pressure of 40 to 50 mm. of mercury in the pneumatic tourniquet has been found to be the most effective, providing the systolic blood pressure is above 100 mm. of mercury. If the patient's blood pressure is below this level a lower pressure should be used in the tourniquet, so that there is a difference of at least 50 mm. of mercury between the systolic blood pressure and the pressure in the tourniquet. Fifth, the cycle should be determined for each case and checked each day the treatment is continued. The tourniquet is inflated with the extremity at the same level as the heart, or in the position it will be necessary to maintain during the treatment. The appearance of the extremity will be waxen at first, but gradually a pinkish color will be seen to creep distalward until it reaches the tip of the digits. The time in minutes required for change in color after inflation of the tourniquet should represent the "on" part of the cycle. In cases in which the change in color may not be so apparent, the time required for the superficial veins of the distal part of the extremity to become engorged should be taken. In the case reported nine minutes was the "on" period determined when treatment was commenced. Subsequently it was reduced to four

minutes as the circulation improved. It is unusual to have such a long period, but this is explicable since the arterial occlusion had been so high and practically complete. If the occlusion is more distal a four to six minute period of occlusion is more desirable. A period shorter than four minutes seldom if ever is to be recommended.

The "off" period is likewise determined by deflating the tourniquet. This should be the time in minutes required for the distal part of the extremity to blanch or the superficial veins to empty of blood. In the case reported a one minute "off" period was used when the treatment was commenced. Later this was increased to two minutes, to correspond with the improvement in the circulation and also to permit the disappearance of the edema which had formed as a result of the long (nine minute) "on" period and the short (one minute) "off" period.

In cases of severe arterial occlusion, such as the case reported, continuous treatment both day and night is recommended until the circulation improves sufficiently to permit rest periods of one to two hours between periods of three to four hours of treatment. In the case reported it was necessary to use an ordinary sphygmomanometer for the tourniquet, since the automatic type of electrically

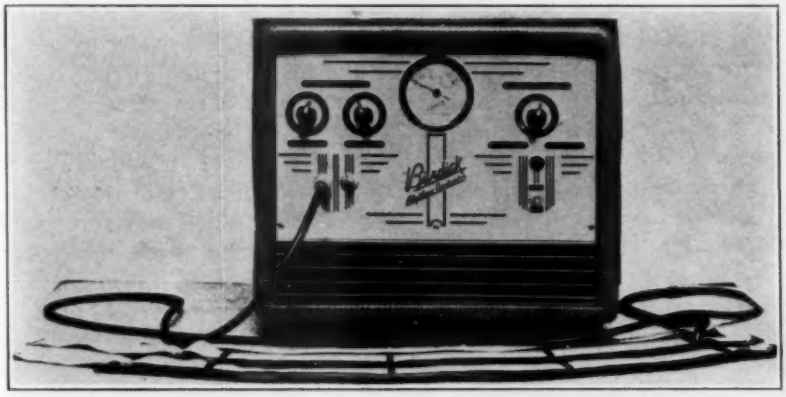

Fig. 7.—A photograph of the Burdick intermittent venous occlusion apparatus. This machine has separate controls which permit "on" periods of one to ten minutes and "off" periods of one to six minutes. By this means any type of cycle can be obtained.

controlled machines did not permit a nine minute "on" and a a one minute "off" cycle. The cuff of the sphygmomanometer was inflated and deflated manually every ten minutes for the first forty-eight hours by the patient's nurses. As the result of experience with this patient it is now possible to get any cycle with an "on" period of one to ten minutes and an "off" period of one to six minutes with the Burdick automatic electrical machine for producing intermittent venous congestion (fig. 7).

In a woman 58 years of age the arterial blood supply to the left leg was interrupted by ligation of the hypogastric artery and occlusion of the external iliac artery secondary to trauma. Adequate arterial circulation was reestablished in the leg and gangrene was prevented by means of intermittent venous occlusion, a long period of occlusion and a short period of release being used. The technic of intermittent venous occlusion for the treatment of acute arterial occlusion is discussed.

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DEMEROL

A SUBSTITUTE FOR MORPHINE IN THE TREATMENT OF POSTOPERATIVE PAIN

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It is the purpose of this paper to present in greater detail a report of the effectiveness of demerol, a new synthetic analgesic, for the control of postoperative pain and restlessness. A complete discussion [1] of the properties of the drug, including its effectiveness, safety and potency in the treatment of a large variety of conditions, has already been presented by one of us (R. C. B.).

Demerol [2] (1-methyl-4-phenyl-piperidine-4-carboxylic acid ethyl ester hydrochloride) was introduced by Eisleb and Schaumann [3] in 1939 and was almost immediately acclaimed by numerous investigators [4] as a potent and safe analgesic approaching morphine in effectiveness. Its advantages, especially its antispasmodic properties, soon became apparent. Thus the atropine-like effect combined with sedative action makes it an ideal drug for the treatment of severe colicky pain. With exception of rare hypersensitive persons, demerol may be used without contraindication in patients with severe anemia, disease of the liver or kidneys or bronchial asthma. Of particular importance is the rarity of occurrence of respiratory depression in patients treated with demerol. This has been noted only three times: once in a group of 1,119 medical and surgical patients [1] and twice in a group of 338 patients receiving the drug for preanesthesia.[5] In each case it occurred in a person over the age of 60 who presented advanced debilitation and cerebral arteriosclerosis. Other advantages and minor disadvantages will be considered in the discussion of the results.

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1. Batterman, R. C.: Clinical Effectiveness and Safety of a New Synthetic Analgesic Drug, Dermol, Arch. Int. Med. **71**:345 (March) 1943; abstracted, Federation Proc. **1**:143, 1942.

2. The Alba Pharmaceutical Company, Inc., New York, has supplied us with the drug and other aid in connection with this investigation. Demerol was introduced in Europe as "eudolat" and was subsequently known on that continent and in South America as "dolantin."

3. Eisleb, O., and Schaumann, O.: Dolantin, ein neuartiges Spasmolytikum und Analgetikum (Chemisches und Pharmakologisches), Deutsche med. Wchnschr. **65**:967 (June 16) 1939.

4. (*a*) Dolle, W.: Dolantin, ein neues Spasmolyticum und Analgeticum in der Gynäkologie, Prakt. Arzt **25**:113, 1940. (*b*) Rosenthal, H.: Beobachtungen zur Bekampfung des Wundschmerzes mit dem neuen Analgetikum, Dolantin, München. med. Wchnschr. **86**:1079 (July 14) 1939. (*c*) Schäfer, F.: Schmerzbekämpfung in der Chirurgie mit Dolantin, Deutsche med. Wchnschr. **65**:970 (June 16) 1939. (*d*) Schlungbaum, H.: Schmerzbekämpfung mit Dolantin, einem synthetisch hergestellten Spasmolytikum und Analgetikum, Med. Klin. **35**:1259 (Sept. 22) 1939. (*e*) Sostmann, H. E.: Zur Ablösung des Morfins und seiner Abkömmlinge in der Gynäkologie durch Dolantin, Med. Welt **14**:325 (March 30) 1940. (*f*) Althoff, H.: Klinische Erfahrungen mit Dolantin-Bayer, Therap. d. Gegenw. **6**:258, 1939. (*g*) Dietrich, H.: Klinische Erfahrungen mit einem neuen synthetischen Spasmolytikum und Analgetikum, Deutsche med. Wchnschr. **65**:969 (June 16) 1939. (*h*) Klein, E. K.: Erfahrungen mit Dolantin; einem myotrop und neurotrop wirkenden Spasmolytikum, München. med Wchnschr. **86**:1674 (Nov. 24) 1939. (*i*) Reisinger, F.: Das neue Analgetikum und Spasmolytikum Dolantin, Wien. med. Wchnschr. **90**:400 (May 25) 1940. (*j*) Heydner, W.: Erfahrungen mit dem Spasmo-Analgetikum Dolantin bei Herzkranken, Fortschr. d. Therap. **16**:33 (Jan.) 1940.

5. Rovenstine, E. A., and Batterman, R. C.: The Utility of Demerol as a Substitute for the Opiates in Preanesthetic Medication, Anesthesiology, to be published.

SCOPE OF INVESTIGATION

The cases of 488 postoperative patients, 165 of whom had had abdominal section, are available for analysis. There was no criterion for the selection of patients other than that they be conscious and cooperative at the time of admission to the surgical ward. The majority of the postoperative patients had received demerol for preanesthesia. The results of this use of the drug are included in another report.[5]

Demerol was dispensed in tablets of 50 mg. each for oral use (research number D-140) and in solution (research number S-140) in ampule or vial so that 1 cc. contained 50 mg. The dose varied between 50 and 150 mg., orally or parenterally, in a single dose or in repeated doses several times daily. In the final analysis the dose and the route of administration were taken into consideration. The same patient may at different times have received varying doses by different routes. A variation may have occurred but once, or repeatedly, over an extended period. The effectiveness of a certain dose, given either orally or parenterally, was considered as an individual trial and recorded as such. For example, 41 patients were subjected to appendectomy. All received demerol parenterally, and 4 were treated in addition with the oral preparation. Among those treated by injection varying doses were tried with 5, so that a total of 46 trials became available for analysis in this group.

CONTROL OF POSTOPERATIVE PAIN

The effectiveness of demerol immediately becomes apparent when its ability to control postoperative pain is observed. Among the 164 patients receiving the drug parenterally during the postoperative period after laparotomy (table 1) 95.5 per cent of the 182 trials resulted in complete, satisfactory relief of the pain, discomfort and restlessness. After procedures other than laparotomy demerol is only slightly less effective (table 2). Thus in 91.5 per cent of 271 trials in 252 cases, postoperative pain was completely controlled. An additional 5.2 per cent experienced a moderate effect or relief for approximately three hours.

The after-effects of rectal operations are notoriously painful, occasionally necessitating the use of large doses of opiates. In this group there was failure to give a satisfactory response to demerol in only 4 instances out of 45 trials, and even in the 4 patients who failed to respond in one trial the subsequent administration of a larger dose resulted in alleviation of the pain.

Regardless of the severity of the condition, the duration of the operation, the age of the patient and the ultimate prognosis, with rare exceptions the administration of 75 to 100 mg. of demerol parenterally every three to four hours, if necessary, was sufficient to make the patient comfortable and facilitate the usual therapeutic procedures. Many patients were in the period of effect of the anesthetic agent, which probably influenced the results to some extent. However, postoperative control of pain was hitherto achieved only by the use of morphine or one of its derivatives.

Orally, demerol was effective when the pain was not severe or after the acute postoperative symptoms had subsided. Satisfactory control of the pain was achieved in approximately 87 per cent of 123 trials on 118 patients (table 3). It is thus possible to continue using and to rely on the oral preparation if the postoperative discomfort should persist for several days.

In the postoperative phase of treatment demerol was found to be a safe drug, rarely causing untoward reactions. The subjective responses of dizziness and nausea, which in two other series [1] were noted in approximately 20 and 8 per cent of the patients respectively, occurred rarely in this particular study. Here again the anesthetic may have influenced the incidence of untoward reactions. The incidence of vomiting was no higher than one would expect after major operations. Comment regarding the rarity of respiratory depression has already been made. Since demerol has been in use in the surgical service there has been no instance of respiratory depression in a postoperative patient. Here obviously is a distinct advantage over the opiates, for respiratory depression resulting from frequent and repeated use of

TABLE 1.—*Effectiveness of Demerol (Parenterally) for Control of Pain and Restlessness Following Laparotomy*

Type of Operation	Number of Patients	Number of Trials	Effectiveness *											
			Complete: Dose, Mg.			Moderate: Dose, Mg.			Slight: Dose, Mg.			None: Dose, Mg.		
			50	75	100	50	75	100	50	75	100	50	75	100
Appendectomy	41	46	3	23	18	1	..	..	..	1	..	..	..	..
Exploratory operation	32	35	1	8	23	1	..	2	..	..	..	..	..	..
Gastrostomy	10	12	2	4	6	..	..	..	..	..	..	..	..	..
Jejunostomy	2	2	1	1	..	..	..	..	..	..	..	..	..	..
Gastric resection	15	15	..	4	10	..	..	1	..	..	..	..	..	..
Repair of perforated peptic ulcer	6	7	..	1	6	..	..	..	..	..	..	..	..	..
Gastroenterostomy	6	6	..	..	6	..	..	..	..	..	..	..	..	..
Cholecystectomy	16	18	1	5	12	..	..	..	..	..	..	..	..	..
Cholecystostomy	6	6	..	3	3	..	..	..	..	..	..	..	..	..
Choledochgastrostomy	1	1	..	..	1	..	..	..	..	..	..	..	..	..
Release of intestinal obstruction	7	10	1	2	6	..	..	..	..	1	..	..	..	..
Colonic resection	8	9	1	4	4	..	..	..	..	..	..	..	..	..
Colostomy	14	15	..	4	11	..	..	..	..	..	..	..	..	..
Total	164	182	10	59	106	2	..	3	..	2	..	..	..	..
Per cent †			95.5			2.6			1.1					

* Different doses may have been used in the same case.
† In terms of number of trials (182) regardless of dose administered.

TABLE 2.—*Effectiveness of Demerol (Parenterally) for Control of Pain and Restlessness Following Operations Other Than Laparotomy*

Type of Operation	Number of Patients	Number of Trials	Effectiveness *															
			Complete: Dose, Mg.				Moderate: Dose, Mg.				Slight: Dose, Mg.				None: Dose, Mg.			
			50	75	100	150	50	75	100	150	50	75	100	150	50	75	100	150
Inguinal herniorrhaphy	44	46	2	13	30	..	..	1	..	..	..	..	..	..	..	..	..	..
Femoral herniorrhaphy	4	5	1	1	3	..	..	..	..	..	..	..	..	..	..	..	..	..
Ventral herniorrhaphy	8	8	..	2	6	..	..	..	..	..	..	..	..	..	..	..	..	..
Thyroidectomy	12	12	..	1	11	..	..	..	..	..	..	..	..	..	..	..	..	..
Radical mastectomy	7	10	..	3	7	..	..	..	..	..	..	..	..	..	..	..	..	..
Sacroperineal resection	5	6	..	2	4	..	..	..	..	..	..	..	..	..	..	..	..	..
Amputation, toes	9	9	..	2	7	..	..	..	..	..	..	..	..	..	..	..	..	..
Amputation, midthigh	7	8	..	2	5	..	..	..	..	..	..	1	..	..	..	..	..	..
Amputation, others	2	2	..	1	1	..	..	..	..	..	..	..	..	..	..	..	..	..
Thoracotomy	3	4	..	2	2	..	..	..	..	..	..	..	..	..	..	..	..	..
Hemorrhoidectomy	41	45	1	4	31	..	1	2	2	..	..	2	..	..	..	2	..	..
Miscellaneous rectal operations	20	22	..	4	16	..	..	..	1	..	1	..	..	..	..	..	..	..
Excision of pilonidal sinus	8	8	..	3	4	..	..	..	1	..	..	..	..	..	..	..	..	..
Incision and drainage	27	27	1	9	14	..	..	2	..	..	..	1	..	..	..	..	..	..
Open reducton of fracture	11	12	..	2	7	..	1	..	2	..	..	..	..	..	..	..	..	..
Bone graft	2	2	..	..	2	..	..	..	..	..	..	..	..	..	..	..	..	..
Skin graft	5	6	..	1	3	..	..	..	..	..	..	..	..	..	1	..	1	..
Incision, miscellaneous	26	27	..	8	17	1	1	..	..	..	..	..	..	..	..	..	..	..
Ligation of saphenous vein	9	9	..	1	8	..	..	..	..	..	..	..	..	..	..	..	..	..
Miscellaneous procedures	2	3	..	1	2	..	..	..	..	..	..	..	..	..	..	..	..	..
Totals	252	271	5	62	180	1	3	5	6	..	1	4	..	..	1	2	1	..
Per cent †			91.5				5.2				1.8				1.4			

* Different doses may have been used in the same case.
† In terms of number of trials (271) regardless of dose administered.

TABLE 3.—*Effectiveness of Demerol (Orally) for Control of Pain and Restlessness Following Operations Other than Laparotomy*

Type of Operation	Number of Patients	Number of Trials	Effectiveness *															
			Complete: Dose, Mg.				Moderate: Dose, Mg.				Slight: Dose, Mg.				None: Dose, Mg.			
			50	75	100	150	50	75	100	150	50	75	100	150	50	75	100	150
Inguinal herniorrhaphy	13	13	3	1	7	..	..	..	2	..	..	..	..	..	..	..	..	..
Femoral herniorrhaphy	1	1	..	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..
Ventral herniorrhaphy	2	2	..	..	2	..	..	..	..	..	..	..	..	..	..	..	..	..
Thyroidectomy	1	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Radical mastectomy	2	2	..	..	2	..	..	..	..	..	..	..	..	..	..	..	..	..
Sacroperineal resection	2	2	..	..	1	..	..	..	1	..	..	..	..	..	..	..	..	..
Amputation, toes	5	5	..	..	5	..	..	..	..	..	..	..	..	..	..	..	..	..
Amputation, midthigh	3	3	..	..	2	1	..	1	2	..	..	..	..	..	1	..	..	1
Hemorrhoidectomy	14	15	1	1	8	..	..	..	1	..	..	..	..	..	1	..	..	..
Miscellaneous rectal operations	6	7	..	..	5	..	..	..	1	..	..	..	..	..	..	..	..	..
Excision of pilonidal sinus	4	4	..	..	3	..	..	..	2	..	..	..	..	..	..	..	..	..
Incision and drainage	22	22	3	1	16	..	..	..	..	..	..	..	..	..	..	..	..	..
Open reduction of fracture	6	8	3	1	4	..	..	..	..	..	..	..	..	..	..	..	..	..
Bone graft	1	1	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Skin graft	3	3	1	..	2	..	..	..	..	..	..	..	..	..	..	..	..	..
Incision, miscellaneous	23	24	6	1	14	..	1	..	2	..	..	..	..	..	..	..	..	..
Ligation of saphenous vein	7	7	2	..	5	..	..	..	..	..	..	..	..	..	..	..	..	..
Miscellaneous procedures	3	3	1	..	2	..	..	..	..	..	..	..	..	..	..	..	..	..
Total	118	123	21	6	79	1	1	1	11	..	..	..	..	..	2	..	..	1
Per cent †			86.9				10.5				..				2.4			

* Different doses may have been used in the same case.
† In terms of number of trials (123) regardless of dose administered.

morphine is a cause for grave concern. With several patients who had received morphine (during the transition period of our study) and in whom respiratory depression had developed, it was possible to continue the administration of demerol for the control of pain without producing this serious side effect.

Of postoperative complications, urinary retention may be most troublesome. Catheterization, especially if repeated at frequent intervals, may result in cystitis or pyelonephritis. The incidence of catheterization among consecutive postoperative patients receiving morphine in one male surgical ward was determined for a period of ten months. During this period 160 operations were performed; 20 patients, an incidence of 12.5 per cent, required catheterization within twenty-four to forty-eight hours postoperatively. In the same ward in the following eleven months, in which demerol was used exclusively, there were 178 consecutive postoperative patients, of whom 14, or 7.8 per cent, required catheterization. There is no doubt that the type of surgical procedure plays a significant role in the development of urinary retention and must be considered in an evaluation of the results just cited. The majority of the patients who were catheterized, whether they received morphine or demerol, had had a rectal operation, a herniorrhaphy or an operation on the lower part of the abdomen. Although the number of postoperative patients is too small and the difference in incidence of urinary retention between patients given morphine and those given demerol may not be statistically significant, it is our belief, nevertheless, that demerol is less likely to produce this undesirable complication. Furthermore, in a group of 812 nonoperative and medical patients urinary retention was noted only once and was not particularly detrimental to the patient's welfare.

In regard to abdominal distention and pulmonary complications we have no data. However, in many patients "gas" pains were effectively relieved. The antispasmodic action of demerol and the lack of constipation may be definite advantages. The drug has little if any action on the cough reflex and hence does not encourage accumulation of bronchial secretions. The dryness of the mucous secretions attributable to its atropine-like action and the bronchial dilatation that it produces are also advantages. The latter is of particular help to patients with bronchial asthma, for whom morphine is contraindicated.

The only disadvantage of demerol as far as postoperative use is concerned is its short action. This, however, is rarely apparent in the first postoperative day. For patients with a protracted and "stormy" course the average dose may be sufficient for only two hours. This may be overcome either by administering the same dose more frequently or by increasing the dose. There is no particular danger of causing undue depression in such cases.

COMMENT

It is our conclusion following these observations on a group of postoperative surgical patients that demerol is a more suitable drug for the control of pain than morphine or any of its derivatives. It has the distinct advantage of rarely producing respiratory depression. Other preferable qualities are its antispasmodic effect on gastrointestinal tract and bronchi, its atropine-like drying action on mucous membrane and its lack of suppression of the cough reflex. It has the relatively unimportant disadvantage of short action, which may be overcome by frequent dosage. The occasional symptoms of dizziness and nausea which have followed administration in other trials were not encountered in this series. These experiences indicate that demerol as a substitute for morphine is equally effective, and safer, for postoperative patients.

Miss Aniele C. Evaskitis, research nurse of the Department of Therapeutics, New York University College of Medicine, assisted in the preparation of this paper.

MISCONCEPTION ABOUT THE "SPRINGINESS" OF THE LONGITUDINAL ARCH OF THE FOOT

MECHANICS OF THE ARCH OF THE FOOT

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From the earliest days of anatomic knowledge the longitudinal arching of the foot has been looked on as designed to provide resilience and has been compared in its shape and function to a spring. This view is expounded in the classic textbooks of anatomy, and has been retained by more contemporary writers, as the term "spring ligament" implies.

The twenty-seventh English edition of Gray's "Anatomy" states:

> The chief characteristic of this [medial longitudinal] arch is its resilience, due to its height and to the number of joints between its component parts. . . . It should be observed that in a normal foot the arches become flattened when erect posture is assumed and are restored when the weight of the body is taken off the feet. This resilience accounts for the suppleness of the normal foot and enhances the value of the arches by rendering possible such rapid and sudden movements as running and jumping.[1]

In the seventh edition of Cunningham's "Textbook of Anatomy"[2] it is written:

> These arches do not merely support the body weight statically as arches of masonry support a bridge: the presence of the joints in the arches introduces a spring mechanism so that the arches resemble the half-elliptical springs of a carriage. They yield slightly when weight is put upon them, and recoil when it is removed. . . . The tension of the plantar calcaneo-navicular ligament, supported by the tibialis posterior muscle, resists the tendency of the weight of the body to drive the head of the talus downwards between the bones which it braces together, and the resilience it imparts to the medial arch is recognised in its common appellation—the spring ligament.

The same interpretation of the function and purpose of arches was given by the more modern authors Callander[3] and Grant.[4] The former stated:

> The ligaments act only as passive agents, in contrast to the muscles which take an active part and are indispensable for the maintenance of the proper shape of the arch. Because of the elasticity of the ligamentous apparatus, the arches flatten out when the foot has to sustain a heavy weight, but they regain their original shape immediately when the weight is removed.

Grant[4] continuously referred to the arches of the foot as "springs." He recommended that the foot be regarded "as a spring rather than as an arch."

Delivered in brief by invitation at the annual meeting of the American Orthopedic Association, Baltimore, June 5, 1942.

From the service of Dr. Leo Mayer, Hospital for Joint Diseases and the service of Dr. J. J. Nutt, New York Polyclinic Medical School and Hospital.

1. Gray, H.: Anatomy: Descriptive and Applied, ed 27, New York, Longmans, Green & Co., 1938, p. 517.
2. Cunningham, D. J.: Textbook of Anatomy, ed. 7, London, Oxford University Press, 1937, pp. 374 and 379.
3. Callander, C. L.: Surgical Anatomy, ed. 2, Philadelphia, W. B. Saunders Company, 1939, p. 802, fig. 442; p. 520, plate 23, figs. 2 and 3.
4. Grant, J. C. B.: A Method of Anatomy: Descriptive and Deductive, ed. 2, Baltimore, William Wood & Company, 1940, pp. 411, 412 and 454.

Figure 373 on page 412 of his book "A Method of Anatomy: Descriptive and Deductive" is intended to illustrate this and also to prove that

> when you place your foot on the ground the spring will, of course, flatten under your weight. . . . At the hinge surfaces between the talus and the navicular and also between the navicular and the three cuneiforms the spring of the arch can flatten and recoil.

Thus it is evident that the arch of the foot has been generally recognized as an elastic recoiling spring from as far back as when the plantar calcaneonavicular ligament was nicknamed "spring ligament" up to the present day.

SPRINGINESS OF THE LONGITUDINAL ARCH OF THE FOOT

The purpose of this paper is to give a critical analysis of this concept. It will first be necessary to consider certain well known mechanical laws.

It is known that the progress of a moving body can be arrested only by application of a sufficient force, or reaction, acting in a direction opposite to that of the movement of the body. The extent of the force necessary to stop a moving body, or as it is called in mechanics the reaction force, depends on the time it takes to bring the body to rest. It is impossible to bring any moving body to rest instantly. Some time, no matter how short, must elapse between the application of the retarding force and the cessation of motion. A greater reaction force must be applied in order to stop a moving body in a shorter time. The degree of shock or resilience which a moving body experiences is controlled entirely by the length of time required to bring it to rest or to change its direction of motion. In other words, the more sudden the stop or change of the direction of motion, the greater will be the shock. Shock absorption or resilience is usually secured in machinery by devices, such as air buffers, rubber pads or steel springs, which possess elasticity —that property of a body which enables it to change its shape under action of a force on it and to resume its original shape when the action of the force is removed. A steel spring or a piece of rubber can be compressed or bent, but it will promptly return to its original form when the force is released.

As an example, consider a half-elliptic spring interposed between the axle of the wheel and the body of a wagon (fig. 1 *A*). When the wheel rides over a prominence in the road it is suddenly pushed upward. The spring flattens and at the same time becomes longer because its anterior and posterior points are separated from each other. Thus the sudden upward motion of the wheel is slowed down by the gradual flattening of the spring, and the shock, which without the spring would be completely transmitted to the body of the wagon, is diminished or absorbed by the spring.

Walking on a stilt is rather jarring, because with each step the downward motion of the body is abruptly stopped the moment the stilt comes in contact with the ground. If, however, a compressible coiled spring (fig. 1 *B*) is incorporated beneath the lower end of the stilt, the time between the contact of the spring with the ground and complete cessation of downward motion of the stilt will be increased, and resilience will be supplied. The degree of resilience depends on the extent of the vertical compressibility of the coiled spring. The longer or higher the coiled spring, the slower will be the stop, and therefore the less will be the shock.

Resilience may also be provided by a half-elliptic curved spring (fig. 1 *C*) attached to the lower end of the stilt. The shock-absorbing action of such a device will depend on the height (h) of the curve. It is obvious, therefore, that the shock-absorbing function of the curved spring is entirely measured by its ability to

flatten. In its turn the flattening of the spring cannot occur unless its ends (S, S) are freely movable against the ground and are able to spread apart in position S', S', when the curve of the spring flattens approaching a straight line.

A somewhat similar shock absorber may be built at the end of the stilt by substituting for an elastic curved spring two pieces made of some comparatively nonelastic rigid material, such as wood or bone, which are hinged to each other in an archlike fashion and connected at their two free ends by some elastic material, such as a tension coiled spring (fig. 1 *D*).

A more complicated shock absorber, built somewhat on the pattern of the human foot, is presented in figure 1 *E*. Several rigid pieces corresponding to the skeleton of the foot are hinged together and connected to each other by coiled springs which correspond to the plantar ligaments and plantar fascia.

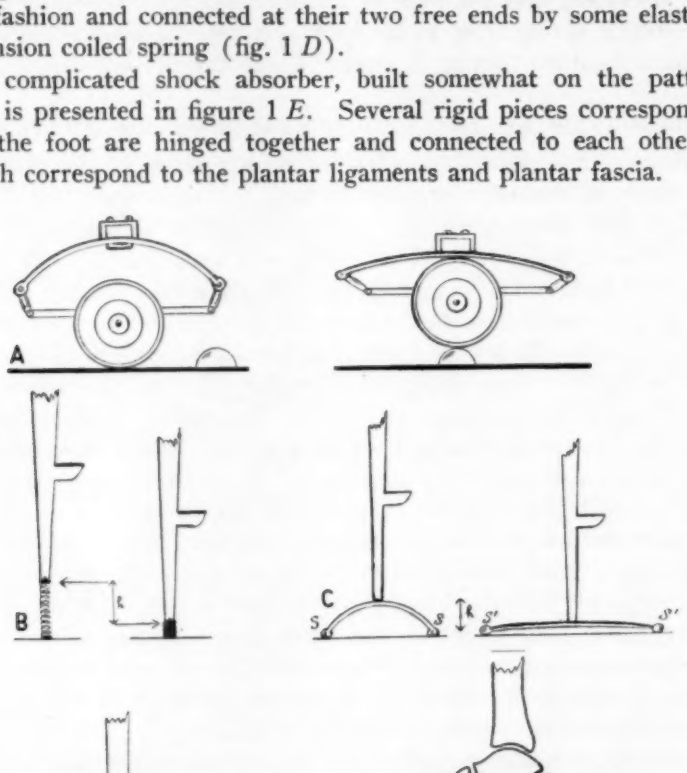

Fig. 1.—*A*, effect of a semielliptic spring interposed between the axle of a wheel and the body of a wagon. *B*, effect of a coil spring attached to the lower end of a stilt. *C*, effect of a half-elliptic spring. *D*, a shock absorber with two rigid arms whose free ends are joined by a coil spring. *E*, a shock absorber made up of several rigid pieces corresponding to the skeleton of the human foot and joined by coil springs.

All that was said in reference to the half-elliptic spring holds true in the case of the rigid wooden shock absorber. The higher its arch, the more resilience it will provide. In addition, two requirements must be fulfilled: First, free mobility must be present in the joints between the separate rigid links of the arch (at least at the joint at its apex); second, each of the ends of the links or at least their two free ends must be connected by some elastic material. Without these neither flattening nor recoiling of the arch would be possible; in other words, the whole device would lose its springiness and become rigid.

Thus, in order that the human foot may possess springiness, it is necessary that the plantar fascia and the plantar ligaments be elastic, or capable of stretching when the weight of the body is borne on the foot and resuming their original length in the non-weight-bearing foot.

According to Gratz,[5] "certain fibrous tissues were found to withstand stress up to a maximum of 1,476 Kg. per square centimeter (20,959 pounds per square inch)" of cross section. Their tensile strength was found to be approximately equal to that of soft steel wire of the same weight. The elasticity of human ligamentous, fascial and other fibrous structures, in the sense of their ability to return to their original shape, was given as more than 500 Kg. per square centimeter (7,100 pounds per square inch), although the elasticity of many tissues exceeded this point. However, the elongation of these structures was negligible, amounting to less than 2 per cent, with tensile load of 100 Kg. per square centimeter of cross section.

The plantar fascia in man is approximately 15 cm. long and has a cross section of at least 0.5 sq. cm. According to precise calculations by Mr. Emilio Pittarelli, an engineer with whom I consulted, the estimated tensile load of plantar fascia is roughly 35 Kg. in a man with average body weight of 60 Kg., standing on one foot in a relaxed position. Consequently, the maximum elongation of the plantar fascia cannot be more than 1.4 per cent of its length.[6] Under such conditions, the plantar fascia may elongate from its original length of 15 cm. to approximately 15.21 cm. This in its turn will allow for sagging of the apex of the longitudinal arch (head of the talus) amounting close to 0.1 cm.

It seems reasonable to assume that the shock-absorbing property of the human foot is only of theoretic interest and of no practical value if "flattening and recoiling" of the arch can take place only within the range of about 0.1 cm. It is evident, then, that the foot is a rigid structure and cannot be compared, as it has been erroneously until now, to a "semielliptic spring."

CONSTRUCTION AND PURPOSE OF THE LONGITUDINAL ARCH

If the longitudinal arch does not provide springiness, what then are its mechanical construction and its purpose?

Man is the only primate who possesses a longitudinal arch; he is likewise the only primate in whom the foot has been perfected for use as a lever in upright bipedal terrestrial progression. It is the writer's belief that the longitudinal arch of the foot was developed in response to functional requirements for increased strength of the foot as a lever.[7]

In designing any structure engineers select materials for the different parts according to the resistance to the particular stresses each part of the structure is expected to bear.[8] In a suspension bridge, as a rule, steel beams are used for the parts under compression stress and cables in places of tensile stress. In the human foot the skeletal parts which possess a great resistance to compression stress and are comparatively weak in tension are analogous to the beams, while the liga-

5. Gratz, C. M.: Biomechanical Studies of Fibrous Tissues Applied to Fascial Surgery, Arch. Surg. **34**:461-495 (March) 1937; Tensile Strength and Elasticity Test of Human Fascia Lata, J. Bone & Joint Surg. **13**:334-340, 1931.

6. It is estimated that if the elongation is 2 per cent with a load of 100 Kg. per 1 sq. cm. of cross section, it will be 4 per cent with a load of 100 Kg. per 0.5 sq. cm. of cross section, and roughly 1.4 per cent with a load of 35 Kg. per 0.5 sq. cm. of cross section.

7. The muscular action will be disregarded for the time being, as for example in the case of a foot with complete paralysis of all the muscles.

8. Stress in mechanics is defined as the result of that part of the force which does not produce motion. If a rubber band is stretched to double its size, part of the force produces motion and the rest (stress) helps to keep the ends of the rubber band apart. Mechanics recognizes tensile stress, which tends to separate particles of material, compression stress, which tends to bring them closer together, and bending stress, which is really a combination of the other two.

mentous tissue, which is able to withstand great tensile stress, is analogous to the cables. It is a well known fact that the bone ruptures first under tension, causing cortical avulsion fracture, while severing of the ligaments is rather uncommon.

If the foot consisted of one solid piece of bone without ligaments it would be subjected to bending stress. In other words, its dorsal bone trabeculae would be subjected to compression and its plantar trabeculae to tension in a manner somewhat similar to the distribution of stresses in a simple beam (fig. 2 *A*). Since the solid bony foot has a comparatively weak tensile strength, it cannot stand much bending and would tend to break.

It is also obvious that no suspension bridge could be built with very elastic cables. Likewise, the ligamentous structures of the foot (such as the plantar fascia, the plantar calcaneonavicular ligament and all the other ligaments of the foot) can withstand a tremendous tensile stress, if the force is applied in the direction parallel to their fibers, without showing any appreciable increase of their length; in other words, their elongation is negligible.

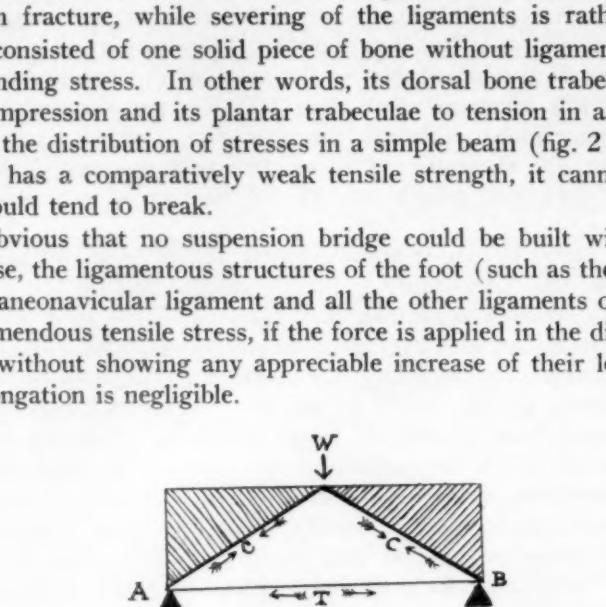

Fig. 2.—*A*, cross section illustrating distribution of stresses in a simple beam. *B*, a simple roof truss. *C*, effect of decreasing the length of a truss. The load on all the members of a truss is inversely proportionate to its height. With the same load, *P*, the compression stress over the struts (*a'c'* and *b'c'*) of truss *C*, and also the tensile stress on its tie rod (*a'b'*) is less than the stresses experienced by the corresponding members of truss *B*, because h_1 is greater than *h*. Therefore, truss *C* is a stronger structure than truss *B* and can withstand a much greater load. Truss *C* is shorter than truss *A* (*a'b'* is smaller than *ab*); consequently, the reaction at the points *a'* and *b'*, being inversely proportionate to the length of the truss, is greater than that over the corresponding points, *a* and *b*.

Engineers build so-called trussed structures in order to avoid bending stresses. A simple beam (*AB*, fig. 2 *A*) supported at both ends and loaded in the middle is subjected to bending stress. Its bottom (solid line *T*) is under tension; the upper part, under compression. The compression forces run diagonally along the solid lines *C*, *C*. The two cross-hatched wedge-shaped portions over the upper part of the beam do not participate in bearing any load. These parts are useless and can be removed for the sake of economy of material and in order to decrease the weight of the whole structure. Thus a simple beam and, likewise, a solid osseous foot are really identical in effect with a truss (figs. 2 *B* and *C*).

Merriman [9] gave the following definition of a truss:

> a jointed structure which is arranged to carry loads in such a manner that each principal member is subjected to stress only in the direction of its length, that is to a tensile or compressive stress, and bending stress is eliminated. . . . In order that a truss may perfectly conform to the above definition it is necessary that the loads should be supported only at the joints, for flexural stresses will result if they are placed at other points on the members. It is further important, in order to secure rigidity, that the elementary figures included between the truss members should be triangles, since a triangle cannot change its shape without altering the lengths of its sides. A rectangular or polygonal figure, on the other hand, may change its shape without altering the lengths of its sides, and hence may be lacking rigidity.

The simple roof truss (fig. 2 *B*) consists of two struts (*ac* and *cb*) which are subjected only to compressive stress running along their length. The tensile stress is entirely taken up by the tie rod (*ab*) connecting the two free ends (*a* and *b*) of the struts, preventing them from spreading apart.

According to mechanics, the load on all the members of the truss (compressive on the struts and tensile on the tie rod) is inversely proportionate to its height (*h*). The higher the truss, the less load will be borne by its members; consequently, the same truss with an increase of its height will be able to withstand a greater load. In other words, the strength of the truss increases proportionately to its height.

Likewise, the reaction at each end (*a* and *b*) of the truss is inversely proportionate to its length (*ab*). In other words, if the length of the truss decreases, the load borne by its ends (*a* and *b*) will increase. The decrease of the length of the truss (provided the length of its struts, *ac* and *cb*, remains the same) actually consists of a shortening of its tie rod (a_1b_1, fig. 2 *C*). It is evident that the truss will become higher if it is shortened ($H_1 > h$, fig. 2 *C*). Therefore, shortening of the truss, with a resultant increase in its height, will also increase the load (reaction) at its end.

If these theoretic considerations of a truss are applied to the "foot truss," it can be understood why a foot with a high arch is stronger than a flat foot; and at the same time why the anterior and the posterior point of support in pes cavus (especially the anterior, represented by the metatarsal heads) bear more weight than in a foot with a low arch.

THE HUMAN FOOT AS A TRUSSED STRUCTURE [10]

The human foot (fig. 3) may be considered to be built as a trussed structure, in which the skeletal parts form struts which are subjected to compression stresses and the plantar fascia acts as a tie rod taking up all the tensile stresses. In this way

9. Merriman, M.: A Text-Book on Roofs and Bridges: Stresses in Simple Trusses, New York, John Wiley & Son, 1914, p. 1.

10. For the sake of simplicity the human foot has been considered as a simple trussed structure. However, according to the analysis of Mr. E. Pittarelli, it would be more appropriate to classify the foot as a rigid frame with a horizontal tie rod. The principal stresses, when the weight of the body is borne, are tension in the tie rod (plantar fascia) and mainly compression in the rigid frame (foot skeleton). However, the compression stresses in the rigid frame (foot skeleton) are distributed on its dorsal side, its plantar side being subjected to tension. This tension is resisted by the plantar ligaments which bind the bones together. That is why the plantar ligaments of the foot are much more powerfully developed than the dorsal ones. If the plantar ligaments were omitted, the rigid frame formed by the foot skeleton would collapse. If the tie rod (plantar fascia) were omitted, the condition of rigid frame without tie rod would develop; then the plantar ligaments would have to take up the entire tensile stress (also that which is normally borne by the plantar fascia). Under such circumstances the load on the plantar ligaments would be too great, and they would be overtaxed.

bending stresses are eliminated, and the strength of the foot as a lever is increased. The higher the "arch," the greater the load that can be borne by the foot truss and the stronger the foot as a lever during locomotion and also in supporting the body in standing. Springiness or flexibility of the foot would, of course, be a mechanical disadvantage in both of these functions. The very flexible foot of the anthropoid apes (gorilla) and the hypermobile weak foot (flat foot) in man may be brought forward as an example of functional deficiency.

The longitudinal arch of the foot cannot be considered as a real arch in the sense used by architects. A typical masonry arch is maintained by its own gravity because of the wedge-shaped form of each stone composing the arch. Each end of the masonry arch must be firmly anchored to the ground to prevent its separation in the horizontal direction. The masonry arch does not require any additional

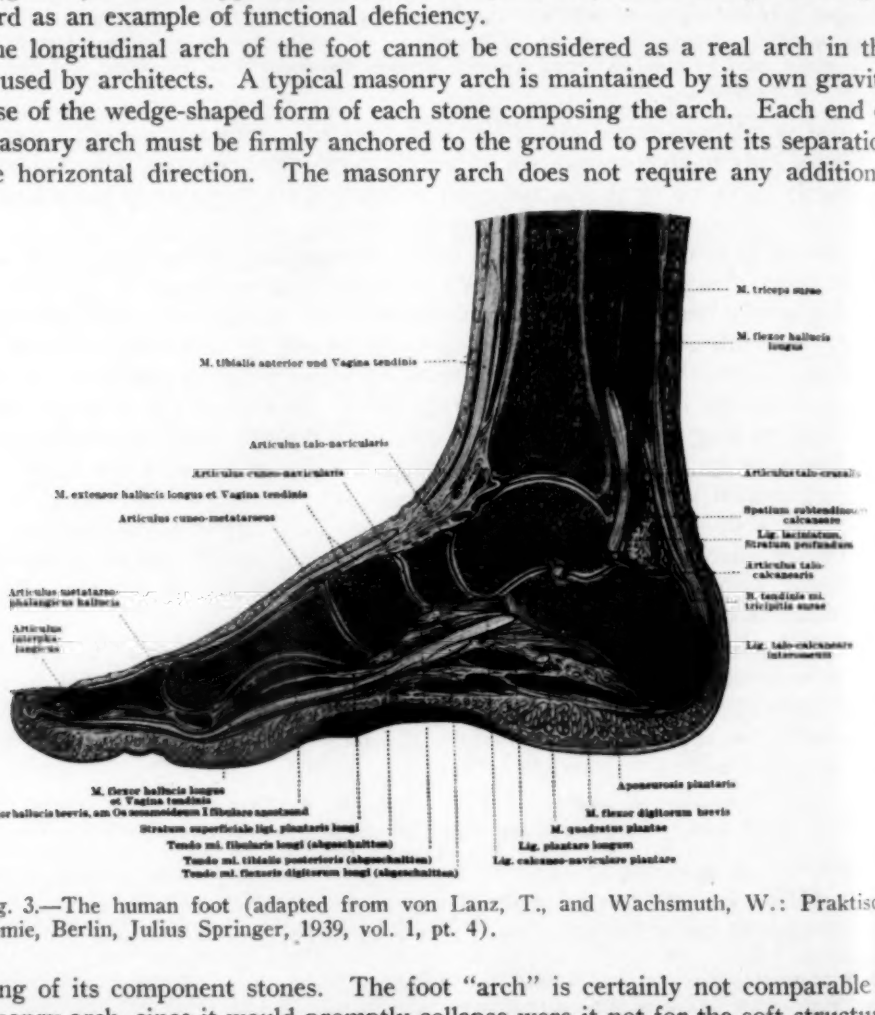

Fig. 3.—The human foot (adapted from von Lanz, T., and Wachsmuth, W.: Praktische Anatomie, Berlin, Julius Springer, 1939, vol. 1, pt. 4).

binding of its component stones. The foot "arch" is certainly not comparable to a masonry arch, since it would promptly collapse were it not for the soft structures (mainly ligaments) which bind together the skeletal parts of the foot.

Thus the apparent "arching" of the foot must be looked on as a result of its construction as a trussed structure rather than a masonry arch. The higher the "arch," the more load can be borne by the foot truss, and therefore the stronger is the foot; and vice versa, the flatter the "arch," the weaker the foot as a lever.

The explanation of the complexity of the foot truss, which is really a combination of several trusses, is found in the well known fact that nature is often not a builder but rather a remodeler. The multiple joints of the foot provided mobility and were necessary for its prehensile functions in man's arboreal ancestors. On descent from the tree to the ground the human foot still retained its many joints, but these have gradually lost their mobility. Thus the foot underwent remodeling,

in that it became more rigid and hence served as a stronger lever. This was a necessary evolutionary step in response to the new functional requirement in connection with adaptation to the upright plantigrade terrestrial stride.

ROLE OF LIGAMENTS AND MUSCLES IN MAINTENANCE OF LONGITUDINAL ARCH

Although it is not within the scope of this paper to go into a detailed discussion of the function of the muscles of the foot, some consideration must be given to their part in maintaining the integrity of the longitudinal arch.

Steindler [11] stated on one page in his book that "the integrity of the form of the foot is entrusted first to its ligamentous and secondly to its muscular apparatus." Nevertheless, five pages later he wrote: "In maintenance of the normal configuration of the foot the muscles stand in first line of defense; the ligamentous resistances are invoked against external forces only after muscular resistance has failed. In other words, the question of equilibrium is, first of all, a problem of muscle tension."

The prevailing opinion as to the dependence of the longitudinal arch upon muscle support was voiced by Sir Arthur Keith,[12] who stated: "The arch of the human foot is safeguarded and maintained by the reflex postural action of muscles, ligaments being merely second line defenses. Flat foot results from a defect in this defense."

Probably the reverse is true. The integrity of the longitudinal arch in the usual standing position depends mainly on the passive tensile strength of the ligaments binding the bones together and on the plantar fascia's acting as a tie rod in the foot truss. The muscles are used to assist the ligamentous structures in locomotion and when the latter are overloaded, as during the lifting of a heavy weight.

In a normal relaxed standing position the muscular action most probably is limited to maintaining a balance between the leg and the foot. A mere muscular tonus may be adequate enough for this purpose. The muscles come into play only in order to keep the weight-bearing line of the body in plumb line so that balance may be maintained by the force of gravity itself, with the least possible expenditure of energy.

The following considerations are advanced in favor of the importance of the ligamentous structures rather than the muscles for maintaining the arch:

1. The height of the longitudinal arch in the weight-bearing foot does not decrease in a fully anesthetized person or in a cadaver with no active muscular function present, and yet the passive support of the ligamentous structure is still available.

2. Flattening of the longitudinal arch would be a logical expectation in cases of complete paralysis of the muscles of the leg and foot if the muscles were more important than the ligaments in support of the arch. However, in many cases of anterior poliomyelitis observed by me in which weight was borne on a foot completely deprived of muscular support and with only the ligaments intact, no appreciable flattening of the longitudinal arch, as compared with that of the opposite unaffected foot, was noted after observation for many years. As a matter of fact, it has been not infrequently observed that the affected foot may sometimes show

11. Steindler, A.: Mechanics of Normal and Pathological Locomotion in Man, Springfield, Ill., Charles C Thomas, Publisher, 1935, pp. 261 and 266.

12. Keith, A.: The History of the Human Foot and Its Bearing on Orthopedic Practice, J. Bone & Joint Surg. **11**:10-32, 1929.

exaggeration of the longitudinal arch (cavus deformity). This may occur in cases in which a trace of power is left in the short plantar muscles, which, being unopposed by the plantar flexors and the dorsiflexors, bring the calcaneal tuber and the metatarsal heads closer together. As a result of this the plantar ligamentous structures become shortened before the patient becomes ambulatory, leading to permanent cavus deformity.

3. Normal standing for more than a few minutes would be impossible because of muscular fatigue if the longitudinal arch were mainly supported by muscular effort. Then usual plantigrade standing would be just as exhausting as standing on the tips of the toes.

4. Nature's design in biomechanical construction always conforms with the rules of economy in material and energy. It is hardly conceivable that such a waste of muscular energy would be permitted.

In the seventh edition of Cunningham's "Textbook of Anatomy," R. D. Lockhart [13] shows lateral roentgenograms of the foot taken in a standing position with muscles contracted and with muscles relaxed as fully as possible. These roentgenograms demonstrate that the longitudinal arch is slightly higher during muscular contraction and that the foot flattens when the muscles are relaxed. Tracings of the roentgenograms prove quite conclusively that simultaneously with the decrease of the height of the longitudinal arch in the state of relaxation, the anterior point of the foot (metatarsal heads) is somewhat more distant from the heel; in other words, the foot shortens on contracture of the muscles and elongates when they are relaxed. Engels,[14] after taking accurate roentgenograms of feet with and without weight bearing, also concluded that the longitudinal arch is slightly higher without weight bearing and becomes lowered when the weight of the body is put on the foot. These observations cannot be looked on as proof that the muscles are the "first line of defense" (Keith [12]) or "indispensable" (Callander [3]) in maintaining the longitudinal arch. If anything, it demonstrates the opposite, namely, that the muscles are subject to fatigue and give way after a short time. Thus the integrity of the longitudinal arch in prolonged standing must necessarily depend primarily on the passive resistance of the ligamentous apparatus.

These considerations likewise do not seem to substantiate the statement of Sir Arthur Keith [12] "that the flat-foot results from a defect in this defense [muscular defense]."

It is true that in walking the muscles come into greater play, because they not only are called on to maintain balance but in addition must lift and propel the whole weight of the body. Since different muscular groups act alternatively, there is a short interval between the muscular contractions allowing rest and restoration of muscular energy. However, even in walking there is a tendency to utilize the passive resistance on the foot truss and the force of gravity, with muscular assistance being employed only when the load becomes excessive.

The intrinsic short plantar muscles, because of their small size and development, need little consideration. They were originally planned to move the toes. They should be looked on as a remnant from the days of prehensile function of the foot, when the toes played a more important role. In the modern human foot the short plantar muscles and, likewise, the toes themselves (except the hallux) show an evolutionary tendency toward retrogressive development; this is especially true of the fifth toe.

13. Lockhart, R. D., in Cunningham,[2] p. 516, fig. 438.

14. Engels, W.: Ueber normalen Fuss und der Plattfuss, Deutsche Ztschr. f. orthop. Chir. **12**:461-503, 1904.

SHOCK-ABSORBING MECHANISM OF THE FOOT

While the "springiness of the arch" must be looked on as highly improbable, there is a definite shock-absorbing function of the foot in locomotion. This is manifested by a certain mechanical arrangement at the talocrural articulation.[15]

There is a phase in walking when one leg is advanced forward with the foot in dorsiflexion (fig. 4 *A*). The body is allowed to fall forward until the heel of the advanced foot comes in contact with the ground. This downward progression of the whole leg column with the superimposed body weight is suddenly stopped by the ground, and shock is produced. The shock can be diminished by increasing the time between the initial contact of the heel with the ground and the complete cessation of the downward progression of the body. This is accomplished by the retarding action of the dorsiflexor muscles of the foot.

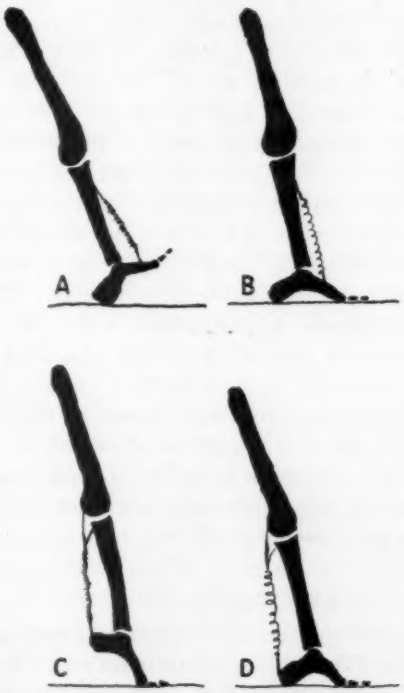

Fig. 4.—Phases in walking. *A*, one leg is advanced with the foot in dorsiflexion. *B*, relaxation of the anterior tibial muscle permits the sole to be placed flat on the ground. *C* and *D*, analogous function of the triceps surae muscle during "toe first" gait or "goose stepping."

For simplicity's sake, let the anterior tibial muscle be considered as representing all of the dorsiflexor muscles of the foot. As the heel touches the ground the anterior tibial muscle is gradually allowed to relax from its original state of full contraction. Thus the ankle is slowly brought down until the entire sole of the foot comes in contact with the ground. In this action the anterior tibial muscle may be compared to a tension coiled spring incorporated between the leg and the foot (fig. 4 *A*). It is clear that this mechanism supplies resilience by increasing the time between the beginning of retardation of motion and the complete stop. The total length of the leg column is originally increased by the length of the heel

15. Mr. John Pinaud, a mechanical engineer, must be credited for the clarification of this mechanical phenomenon and some other points concerning the mechanics of the foot.

bone, since the latter becomes almost vertical in complete dorsiflexion of the foot (fig. 4 *A*). As the foot is slowly lowered, the total length of the leg column gradually diminishes up to the point when the entire sole rests on the ground and the heel resumes its horizontal position (fig. 4 *B*). The jarring "steppage gait" of the patient with paralyzed dorsiflexor muscles of the foot (drop foot) can be easily understood as resulting from lack of retarding action of these muscles. The same holds true after Pirogoff's amputation, when there is no ankle joint to absorb the shock.

A somewhat similar condition is present during "toe first" gait or "goose stepping." In this instance the triceps surae muscle supplies the retarding action instead of the anterior tibial muscle (figs. 4 *C* and *D*).

The triceps surae muscle also plays an important role in retarding the downward progress of the body during jumping from a height. It is well known that landing on the toes at the end of a jump is less jarring than landing flat on the entire sole or on the heel. Landing on the sole or the heel is the most common cause of fracture of the calcaneum, which sometimes is also associated with a fracture of the vertebral bodies. Landing on the toes provides more resilience than landing on the heel, because the toes, or rather the metatarsal heads, are farther from the axis of the ankle joint than the calcaneal tuber. Consequently, the ankle joint is in a much higher position when the toes first touch the ground with the foot in equinus than when the foot is in calcaneus and the tuber calcanei is the first to come in contact with the ground. As a result of this the retarding time is greater when the jumper lands in equinus. Besides, the much more powerful plantar flexor muscles, as compared with the dorsiflexor muscles, are better able to supply retarding springlike action when the landing is made in the equinus position.

In addition to the shock-absorbing mechanism of the ankle joint, a great part of the resilience during the act of jumping is provided by the knee and hip joints. The latter are gradually allowed to go into flexion, the time between the beginning of retardation and a complete stop thus being increased. That is why jumpers are taught to end a jump in a squatting position.

IDIOPATHIC FLAT FOOT

To the best of my knowledge no one has as yet proved or even demonstrated satisfactorily any muscular "defect" or abnormality in the case of idiopathic "flat foot." It has been my progressively strengthening conviction that the idiopathic "flat foot" is a congenital and often hereditary deformity. It must be looked on as an arrest of the ontogenetic development of the foot. In other words, the "flat foot" of an adult has failed to reach the stage of maturity corresponding to the person's age. One of the main characteristics (among many others which cannot be discussed here) of the adult "flat foot" (before the onset of the secondary pathologic changes) is an extreme hypermobility due to ligamentous laxity. Marked ligamentous laxity is also present in the foot of the human embryo and during the first postnatal years. Likewise, the foot of the other primates close to man exhibits even more pronounced hypermobility of the joints of the foot with ligamentous laxity. Thus the idiopathic "flat foot" is usually present at birth and decreases with age. In my opinion the possibility of the acquisition of this deformity or the flattening of the longitudinal arch with age in cases of idiopathic "flat foot" is doubtful. Traumatic, paralytic and inflammatory "flat foot," of course, are excluded from this rule, since they may develop in a normal foot.

SUMMARY AND CONCLUSIONS

1. The human foot is a rigid lever, possessing no "springiness" (of any practical value), as is commonly believed.

2. The ligamentous structures of the foot have a definite elasticity in the sense that they are able to stretch and to resume their original length. However, the amount of elongation of the ligaments when put on stretch is insignificant, and therefore for practical purposes they can be considered as nonyielding structures. This makes improbable the generally accepted concept of the ability of the longitudinal arch to flatten under load and recoil after weight is removed. Consequently, the similarity of the longitudinal arch to "the half-elliptical spring of a carriage" must be incorrect.

3. The formation of the longitudinal arch, which is an exclusive property of the human foot and is not present in any other primates, must be looked on as a tendency to strengthen the human foot as a lever in response to functional requirements in connection with upright bipedal terrestrial progression.

4. The longitudinal "arch" of the human foot cannot be considered as a real masonry arch. The apparent arching of the foot is just one of the results of the foot being built as a trussed structure. By virtue of the trussed construction of the foot, the bones are called on to bear mostly the compression stresses and the ligamentous structures the tensile stresses, bending stresses being completely eliminated in a truss. Such a distribution of stresses is mechanically sound, since the bones have a great resistance to compression, the ligaments to tension. The trussed construction of the human foot contributes greatly to its strength and economy of material.

5. The ligaments are mainly responsible for the integrity of the longitudinal arch. They bind together the bones of the foot in a trussed structure, the plantar fascia acting as a tie rod of the truss.

6. In normal relaxed standing the muscles form a second line of defense in support of the longitudinal arch (or a foot truss). They simply maintain the balance between the leg and the foot by keeping the weight bearing line in the plumb line. They assist the ligaments when the latter are overloaded, as in standing with a heavy load, and of course are active during locomotion.

7. Idiopathic "flat foot" is most probably a congenital and often a hereditary malformation due to arrest of the ontogenetic development and not to faulty muscular function.

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REVIEW OF UROLOGIC SURGERY

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KIDNEY

Anomaly.—Gutierrez [1] drew attention to the clinical indications for division of the renal isthmus in cases in which the diagnosis of horseshoe kidney has been made urographically. First are those in which there are no symptoms and in which the condition is discovered accidentally at operation; in these no surgical treatment is called for. Second are those in which horseshoe kidney is associated with urologic conditions, consisting of urinary symptoms of various kinds, with indefinite abdominal or lumbar pain and with reflex gastrointestinal disturbances, all chronic or recurring in acute attacks. These are the cases in which division of the renal isthmus is indicated for restoration of normal anatomic relationships, relief of pressure on important vessels and nerves and restoration of proper renal drainage. They constitute the great majority of clinical cases. Third are cases in which some kind of gross associated pathologic process is present in half the fused organ, for which heminephrectomy is indicated. Fourth are cases in which gross pathologic conditions are present in both halves of the fused organ, so that some kind of conservative operation, based on the degree of functional activity of each kidney, is called for.

The cases in the second group are those in which the kidneys can be restored to normal function by simple division of the renal isthmus followed by nephropexy on one side or, occasionally, on both sides. In this group the condition constitutes what Gutierrez has elsewhere described as "horseshoe kidney disease," since a very characteristic picture is presented. The principal indications for division of the isthmus after the diagnosis has been made are analyzed.

1. Gutierrez, R.: Operative Technic for Division of Renal Isthmus in Horseshoe Kidney, Am. J. Surg. **55**:28-36 (Jan.) 1942.

The main points in the operative technic of division of the isthmus in horseshoe kidney are, according to Gutierrez, a transverse lumboabdominal incision, which will permit good exposure of the isthmus; an extraperitoneal approach to the kidney; mobilization of the kidney to be operated on by complete nephrolysis and ureterolysis; clamping and ligation of accessory blood vessels of the isthmus; double clamping of the isthmus before the renal parenchyma is divided; closure of raw surfaces by the placing of mattress sutures over interposed fat to prevent hemorrhage; pushing of the other kidney away from the midline to secure outward rotation; carrying out of nephropexy of the kidney operated on, with decapsulation of the upper pole and fixation also of the lower pole to the lateral lumbospinal muscles to provide a rotated position for the securing of adequate drainage; closure of the wound as in ordinary nephropexy, with or without the institution of drainage. Surgical results should be checked by cystoscopic examination and the making of bilateral retrograde pyelograms, which should be repeated two or three weeks after operation. In some cases the performance of nephropexy on the kidney of the opposite side subsequently will be indicated in the pyelograms made during reexaminations, to relieve pain and secure good drainage from that kidney. Gutierrez said that the excellent surgical results obtained demonstrate the value and feasibility of this conservative procedure.

Ectopia.—Laughlin [2] reported a case of renal dystopia (ectopia). Three additional members of the patient's immediate family (her baby, her mother and her sister) presented similar abnormalities. From the urologic standpoint, in his opinion, the case presents an example of an interesting class of renal anomaly; from the gynecologic standpoint, it presents a problem in differential diagnosis; from the obstetric standpoint it presents a possible complication for the pregnant period and a threat to parturition. Laughlin included a brief review of the literature on the etiology, incidence, anatomic and symptomatologic aspects, diagnosis and treatment of this condition.

McCrea [3] stated that the occurrence of congenital solitary pelvic kidney (congenital solitary pelvic renal ectopia) is rare. He said this condition was first described by Hénot in 1830. To date, only 34 previously reported cases are on record. Stevens, in a review published in 1937, estimated that ectopic kidneys were found once in 500 to 1,100 necropsies, whereas true pelvic kidneys occurred once in from 2,150 to 3,000 necropsies. Single kidney, or unilateral renal agenesis, occurs in a ratio of 1 to 700 to 1,610 necropsies, and he estimated that from 4 to 5 per cent of the single kidneys reported were true pelvic kidneys. Stevens concluded, then, that if solitary kidney occurs once in every 1,000 necropsies, solitary pelvic kidney would occur about once in every 22,000 necropsies.

Because of the anatomic position of solitary pelvic kidney, pathologic changes referable to the urinary tract reach a greater proportion relatively earlier in the life of the patient than do the usual anomalies of the kidney. In only 1 case reported has the patient been older than 47 years.

McCrea said that in Hinman's opinion complete absence of a kidney is best explained by the failure of the ureteral bud to develop, rather than by absence of the mesonephric blastoma, and early degeneration of the ureteral bud is a possible cause of complete absence of the kidney.

The high percentage of genital anomalies in the reported cases—17 anomalies in 35 cases—clearly demonstrates that an embryologic association exists between

2. Laughlin, V. C.: Renal Dystopia (Ectopia): A Report of an Interesting Case and Brief Review of the Literature, J. Urol. **47**:632-641 (May) 1942.

3. McCrea, L. E.: Congenital Solitary Pelvic Kidney, J. Urol. **48**:58-68 (July) 1942.

the müllerian and the wolffian duct, McCrea said. The apparent high mortality rate among patients having a solitary pelvic kidney is significant, and it is imperative that all diagnostic data possible be procured before surgical intervention on the kidney is attempted. In view of the difficult position of the kidney, the fact that the blood supply in the presence of this condition is abnormal and the mild degree of hydronephrosis that usually is present because of impaired drainage, surgical treatment should be undertaken only after meticulous and exhaustive diagnostic procedures have been completed.

McCrea reported a case in which congenital solitary pelvic kidney afflicted a man 33 years old. The "kidneys" were found to consist of a single fused structure lying in the hollow of the sacrum. The mass was roughly ovoid, although it could be considered to have a right and a left component. Only one ureter was present; it arose from a single pelvis and entered the bladder 1.5 cm. behind and to the right of the vesical orifice. There was no evidence of a left ureteral opening. The bladder was otherwise normal. Two vessels furnished the blood supply of the kidney.

Hydronephrosis.—Ballenger and McDonald [4] stated that many hydronephrotic kidneys are needlessly sacrificed because of inadequate diagnosis of the causative lesion and failure to correct anatomic defects by proper surgical procedures. Correct diagnosis cannot be arrived at without the making of a clearcut ureteropyelogram and a roentgenogram with the patient in the upright position. Proper surgical procedures should be aimed toward correction of the obstructing lesion. This lesion may be an anomalous blood vessel, or it may take the form of adhesive bands or valvular formations. In addition to correction of the obstruction, excision of the redundant pelvic sac should be carried out. Drainage of the reconstructed pelvis and splinting of the ureter for two weeks or longer are second in importance only to relief of the obstruction. Nephropexy is required in most instances.

Lieberthal [5] reported a case of giant hydronephrosis. In 1935 Howze was able to collect from the literature 32 such cases in which the capacity of the sac varied from 1 to 50 liters. In most cases the condition occurs in children or young adult persons whose average age is from 25 to 30 years. The predominant clinical observation is that of a large abdominal mass. Usually, there are a few symptoms referable to the urinary tract. These large sacs rupture easily.

In Lieberthal's case the patient was a 3 year old girl. An abdominal swelling had been present since the first year of life. Physical examination disclosed a protuberant abdomen. On abdominal palpation, a large, tense, globular mass was felt, which filled the right half of the abdomen and extended well over the midline to the left. A retrograde pyelogram showed the mass to be a large right kidney. Nephrostomy was done, and 2,700 cc. of fluid was aspirated. Ten days later nephrectomy was carried out successfully.

Sauer [6] reported a case in which massive hydronephrosis occurred in a boy 16 years old. Examination revealed that tenderness and rigidity of the epigastrium extended down to the left lower portion of the abdomen. On abdominal exploration a large fluctuant mass was discovered. This was tapped with a small needle, and straw-colored fluid was removed. Later, cystoscopic examination confirmed the diagnosis of massive hydronephrosis of the left kidney. Nephrectomy was performed, and the specimen which was removed was filled with 3,800 cc. of fluid.

4. Ballenger, E. G., and McDonald, H. P.: Conservation of the Hydronephrotic Kidney, J. Urol. **47**:203-208 (March) 1942.

5. Lieberthal, F.: Giant Hydronephrosis, J. Urol. **48**:23-26 (July) 1942.

6. Sauer, H. R.: Massive Hydronephrosis: Report of One Case, J. Urol. **47**:416-420 (April) 1942.

Ercole [7] reported 3 cases of traumatic pseudohydronephrosis in children between the ages of 3 and 7 years, on all of whom he had had the opportunity to operate. He said that Legué defined the clinical picture of traumatic pseudohydronephrosis as a condition which appears relatively late after rupture of a kidney, generally after the lapse of fifteen to twenty days, at a time when it might be supposed that the traumatic process had passed off, and as a condition characterized by an insidious evolution without any general symptoms and with few local signs. This was the course in all 3 of Ercole's cases. The rarity of this complication is held to be due to the fact that for it to develop there must be rupture not only of the parenchyma but also of the excretory passages or a type of rupture that causes sectioning of the ureter—traumatism so grave that the surgeon ordinarily operates immediately, before there is time for the formation of what Ercole called a uro-hematic collection.

In those exceptional cases in which the patient does not come to immediate operation, the history is substantially as follows: After traumatism to the kidney has occurred which causes hematuria of variable intensity, a free period intervenes, which may last for a few days or for two to three weeks, at the end of which the patient complains of pains in the lumbar fossa. As a rule these pains are of only moderate degree. Examination will reveal a tumefaction which suggests the existence of a retroperitoneal fluctuant tumor. Ercole said the diagnosis lies somewhere between hydronephrosis and traumatic pseudohydronephrosis but is oriented toward the latter condition by the relatively short time that has elapsed since the traumatism occurred. Results of catheterization are negative; the ureteral catheter encounters an obstacle at some point in its course and this obstacle prevents evacuation of fluid. In most cases retrograde pyelography is for the same reason a failure, but in some instances when such pyelography is used the cavities can be filled and the site of the rupture of the kidney can be seen. Finally, the excretory urogram may serve to clear up the diagnosis, as it did in Ercole's first case, in which the cavities of the kidney were seen clearly not to be dilated, so that it was possible for him to discard the diagnosis of "true hydronephrosis." The existence of a "free" interval between the trauma and the formation of the collection disposes of the possibility of a perirenal hematoma, in the absence of the local and general symptoms that usually accompany the latter lesion.

A roentgenologic sign to which Ercole attributed great importance is the haziness of the shadow of the psoas muscle; such haziness was present in all his 3 cases as well as in several patients with spontaneous pseudohydronephrosis whom he had the opportunity to observe.

Ercole said that treatment should be conservative whenever this is possible, although in a large number of cases nephrectomy is the only recourse. In 1 of his cases he was able to do a conservative operation, consisting of suture of the ureter; the results were still in doubt at the time of his report, because the patient had been seen very recently, and he said that a few months would have to pass before the results could be checked urographically. In the other 2 cases, nephrectomy was necessary.

Stone.—Lich and Mansfield [8] discussed urinary calculi in relation to the factor of recumbency of the patient and reported 4 cases. The etiology of renal calculi is a complex and controversial subject. When a bone is not used, it undergoes a

7. Ercole, R.: Pseudohidronefrosis traumática a propósito de 3 observaciones de la infancia, Rev. argent. de neurol. **10**:671-679 (Nov.-Dec.) 1941.

8. Lich, R., Jr., and Mansfield, R.: Urinary Calculi and Recumbency, Am. J. Surg. **57**: 89-93 (July) 1942.

loss of some of its calcium salts, and when the muscular system is put at rest muscular atrophy occurs, with a concomitant reduction in the blood supply. Therefore, the reduced supply of blood to the muscles creates a relative hyperemia of the bone, and this hyperemia in turn promotes rarefaction. Although calcium is not excreted primarily through the kidney, the content of calcium in the urine is markedly increased during a period of decalcification of bone. In the event that the urine becomes highly concentrated, the calcium salt may reach a point of supersaturation and initiate a precipitate of inorganic calcium. A so-called mudstone is thus formed in the renal pelvis, the ureter or the bladder. If conditions are favorable, additional calcium is precipitated and the calculus increases in size until it may fill the entire renal pelvis and finally impair renal function. The mechanism of precipitation of salt from a saturated solution is effective in the production of calculi during the patient's recumbency, since most of the stones are composed of calcium phosphate. The role of infection in the precipitation of urinary salts is not a factor in this particular circumstance, according to Lich and Mansfield, since a large proportion of the renal stones which develop during recumbency of a patient are found in sterile urine.

Hematuria is the foremost symptom of urinary calculi associated with the type of recumbency under discussion. Hematuria usually is first manifest when the patient's position is radically changed. Renal colic, another manifestation of urinary stone, generally is accompanied by microscopic hematuria. However, in the presence of renal stone associated with enforced recumbency of a patient, renal colic is far less common than is hematuria.

The prevention of renal stones is, of course, the prime consideration. It has been demonstrated repeatedly that uninfected renal calculi in the recumbent patient can be dissolved by the maintenance of an acid urine. Lich and Mansfield expressed the opinion that it follows that in the absence of infection the formation of stones can be prevented. Decalcification of bone must be kept at a minimum. Decalcification can be reduced best by active movement of the parts of the patient's body not involved by the primary pathologic process, and massage of the affected parts affords protection from local hyperemia of bone and consequent decalcification of the bone.

The fluid balance of the patient must be carefully controlled, so that the urinary precipitation of salt is prevented. The patient must take at least 2,500 cc. of liquid daily and must take more if the loss of fluid is great because of such an added factor as fever, diarrhea or vomiting. The dietary regimen must be carefully planned throughout the entire course of the patient's recumbent period. Since the diet must produce an acid ash, the ingestion of proteins is of very definite importance. Meats, fish and cereals should be included in the daily diet, and vegetables and fruits should be intelligently employed, since they produce an alkaline urine. Fluids administered must be those which will yield an acid ash, for it would be sheer folly to advise an acid ash diet and then to permit the free taking of fluids which will produce an alkaline ash. Repeated urinalysis is an essential part of the medical regimen. At weekly intervals the hydrogen ion concentration of the urine should be determined, and, at intervals certainly no longer than a month, microscopic examination of the urine should be carried out, so that thereby a stone can be discovered long before it has produced subjective manifestations. At intervals not longer than forty-eight to seventy-two hours the patient must be made to change position completely. Lich and Mansfield said that unintelligent use of the urethral catheter is positively contraindicated among patients whose long recumbency is anticipated.

Calcium Plaques.—Vermooten [9] discussed the origin and development in the renal papilla of what have come to be known as "Randall's calcium plaques." He said that a change, identical with that which takes place during the origin and development of bone, occurs in the renal papilla but pointed out that this change rarely goes beyond the stage of deposition of calcium salts. This pathologic process, like the pathologic deposition of calcium elsewhere in the body, is most commonly associated with senescence and the gradually failing circulation which accompanies senescence.

Injury arising from any other cause than the one in question may be responsible for localized zones of calcification, Vermooten said, but cannot account for the generalized distribution of calcium so commonly seen in renal papillae, especially when Randall's calcium plaques are present. This deposition of calcium salts takes place in any of the collagen fibers in the renal papillae. It may thus be seen in the interstitial connective tissue, in the basement membrane of the collecting tubules or in the circular (spinning) fibers surrounding the small blood vessels and capillaries. Any of these zones of calcification, when it is situated immediately subepithelially, may ulcerate through the epithelium of the renal papilla and so form one of Randall's plaques. Injury to the lining epithelium of the collecting tubules by toxins and the like is quite incidental, Vermooten stated, and, although it may do so, does not necessarily play an important part in the formation of Randall's plaques.

Tumor.—Forsythe [10] reported a case of bilateral hypernephroma of the kidney. He said that a review of the literature revealed only 6 cases in which bilateral primary hypernephroma had been diagnosed and that in some of these cases the diagnosis seemed to him to be questionable. In Forsythe's case the patient was a 62 year old man who had complete urinary retention that had followed an episode of hematuria of several days' duration. Excretory urograms showed only fair excretion of dye on the left and no excretion on the right. Because of bleeding and elevation of the values for nonprotein nitrogen, the operation selected was suprapubic cystostomy. One week later excretory urograms were again made. A diagnosis of tumor of the right kidney was made. Removal of the right kidney was performed, after supportive therapy including the transfusion of blood had been carried out, and a kidney extensively involved by a tumor was removed. The patient died of cardiac failure forty-eight hours after the operation. Necropsy revealed that a tumor 4 by 6 cm. also had been present in the midportion of the left kidney. This tumor appeared to be a separate primary lesion.

Prince [11] reported a case of primary angioendothelioma of the kidney. He said that tumors of this type are very rare in the urinary tract; several have been reported as arising in the corpora cavernosa of the penis and in the testis and the ovary. In Prince's case the patient was a 51 year old man who complained of a dull ache in the left flank which he said had been present for two weeks. Ten years previously he had experienced a similar type of pain and gross hematuria. Cystoscopic examination indicated that hydronephrosis was present on the left, and nephrectomy was done. On removal of the kidney, it was found that instead of being large and hydronephrotic, as the pyelograms had suggested, it was small and firm and contained a tumor. The diagnosis was "angioendothelioma of the kidney."

9. Vermooten, V.: The Origin and Development in the Renal Papilla of Randall's Calcium Plaques, J. Urol. **48**:27-37 (July) 1942.

10. Forsythe, W. E.: Bilateral Hypernephroma: Report of a Case, J. Urol. **47**:784-786 (June) 1942.

11. Prince, C. L.: Primary Angio-Endothelioma of the Kidney: Report of a Case and Brief Review, J. Urol. **47**:787-792 (June) 1942.

Castaño, de Surra Canard and Ortiz [12] presented a case in which the symptomatologic aspects of lithiasis had caused them to overlook a neoplasm, a more important disease, which was also present. About seven years previously the patient had felt a sharp pain in the left lumbar region, with extension to the testis on the same side, accompanied by hematuria and fever. Three years later the same clinical picture recurred. All that had been discovered at this time was stricture of the urethra for which dilation was carried out. The painful attacks with hematuria had increased in frequency and had brought the patient to the hospital for observation and treatment. He had a varied history of genitourinary disturbances involving the lower part of the tract. He had frank dysuria, which would disappear if he assumed the dorsal decubitus position during micturition.

A plain roentgenogram disclosed two dense shadows, one in the left kidney and one in the bladder, both of which appeared to be of the same nature and to be caused by calculi. Excretory urograms revealed the same shadow in the left kidney, but in these urograms it appeared to be larger and prolonged downward and outward. After cystoscopic examination and dilation, the calculus in the bladder was finally crushed and the fragments were eliminated spontaneously. On exploration of the left kidney, small serpentine angiomatoid veins of vermiform appearance, forming a plaque 7 cm. in diameter, were found under Zuckerkandl's fascia. When the kidney was freed, large and friable veins which bled freely were found to emerge from the parenchyma, and on removal of the plaque the veins of the parenchyma itself were seen to be of the same character. A diagnosis of malignant renal tumor was made, and nephrectomy was carried out. Histologic examination revealed a clear-celled epithelioma.

Castaño, de Surra Canard and Oritz said that such association of lithiasis and a malignant process within the kidney is infrequent; they expressed the belief that the incidence varies between 5 and 20 per cent, these estimates including malignant tumors of both the pelvis and the parenchyma. Two theories are offered in explanation of the point of the union of these two entities. According to one, prolonged irritative action of the stone on the renal pelvis or on a calix is a predisposing element that can give rise to the neoplasm. According to the other, the stone is regarded as a result of the neoplasm; that is, the stone is formed by the lithogenic precipitation of tumoral detritus. Castaño, de Surra Canard and Ortiz said that they hold the former view in respect to the case they presented.

Cysts.—Gutierrez [13] presented a clinicoanatomopathologic classification of cystic conditions that may be found in the kidney or in the region near that organ, in which he emphasizes the fact that different types of large solitary cysts can be grouped according to number, size and anatomic location, as well as by type of the lesion and nature of its contents. Three main types are demonstrable urographically and anatomopathologically as follows: (1) The cyst is connected with a calix or the renal pelvis; (2) the cyst is not so connected but lies within the structure of the kidney, and (3) the cyst lies outside the structure of the kidney but within the region of the organ. Such cysts may be congenital or acquired. Their pathogenesis, however, remains uncertain, although some form of obstruction or trauma in the uriniferous tubules is believed always to play a part, in that it causes retention. The cysts appear most frequently at the age of the patient at which arteriosclerosis begins. They are frequently associated with some form of congenital renal anomaly. In most cases no symptoms appear until the cyst has

12. Castaño, E.; de Surra Canard, R., and Ortiz, A. A.: Cáncer de riñon y litiasis urinaria asociada, Rev. argent. de urol. **10**:625-630 (Nov.-Dec.) 1941.

13. Gutierrez, R.: Large Solitary Cysts of the Kidney: Types, Differential Diagnosis and Surgical Treatment, Arch. Surg. **44**:279-318 (Feb.) 1942.

attained a size sufficient for it to exert pressure on other abdominal organs. Then pain, dull or acute, abdominal or lumbar, is noticed. A cyst at the upper pole of the kidney may masquerade as a lesion of the liver and gallbladder. Gastrointestinal symptoms frequently dominate the picture. Since the cyst, except in rare instances, does not open into the renal pelvis or a calix, it is usual to find no symptoms referable to the kidney. This accounts for the infrequency with which the correct diagnosis was made in the past, before the use of pyelography and roentgenography became general. However, a cyst of large size may compress the urinary passages and cause symptoms within the urinary system. Hydronephrosis and pyonephrosis are not infrequent. Hematuria may appear, with no other assignable cause. On the basis of study of 10 cases, Gutierrez concluded that the condition can be diagnosed urographically, even in the absence of renal symptoms, whenever the cyst by compression has produced painful symptoms or the physical signs of a tumor mass palpable in one or the other side of the abdomen. He said that the most common roentgenographic and urographic observations are: (1) compression of the renal pelvis or one calix or more, (2) change in the position of the axis of the kidney, (3) inward displacement of the ureter, (4) displacement or rotation of the renal pelvis upward or downward, (5) visualization of the shadow of the cyst, (6) crescent shape of the renal pelvis or the calix, (7) calcification of the walls of the cyst in some cases, (8) visibility of the psoas muscle through the walls of the cyst, (9) shadow of the cyst superimposed on the shadow of the kidney and (10) visualization of the cyst furnished by pyelovenous backflow.

Experience shows, Gutierrez observed, that occasionally a malignant tumor is concealed within the walls of the cyst. This fact, illustrated in one of his own cases, justifies the insistence on open surgical exploration to verify the diagnosis and on removal of the cyst by a conservative operation when possible or by a radical procedure when necessary. When a tumor of the kidney is present the pyelogram as a rule discloses more extensive invasion of the calices and renal pelvis, since in increasing in size a tumor tends to spread outward. The pyelogram of a tumor also presents a more disorganized and bizarre appearance; it follows no such rule of uniformity as does the pyelogram of a simple cyst. In the case of a cyst, he pointed out, the shadow of the kidney itself usually is not enlarged.

In this series of 10 cases, 4 patients were operated on, with curative results. In 1 of these, the cyst was removed from the upper pole, and this procedure was followed by nephropexy on the right. In 2 of the 4 cases extraperitoneal lumbar nephrectomy was done and in the fourth case transperitoneal nephrectomy was performed. In all instances gratifying results were obtained. Of the 6 patients not operated on, the condition of 3 was improved and 3 were not followed. The youngest patient was 18 years old, and the oldest was 74. Five were women, and 5 were men. The diagnosis in 4 cases was made with the aid of intravenous urography and in 4 others with the aid of retrograde pyelograms. In the 2 remaining cases urography did not reveal the cyst and the diagnosis was made during operation for nephropexy. The cyst was situated in the upper pole of the right kidney in 2 cases, in the upper pole of the left kidney in 2, in the lower pole of the right kidney in 3 and in the lower pole of the left kidney in 3. Gutierrez said it was striking to note that in the 2 cases in which the diagnosis had not been made preoperatively the patients were women in whom the right kidney was low in position and readily palpable, and the urographic studies revealed marked pyelectasis, caliectasis and evidence of pyelonephritis and right nephroptosis. In 1 of these 2 cases the cyst was situated in the upper pole of the right kidney, and in the other case it was situated in the lower pole of the right kidney. Resection of the upper pole followed by nephropexy sufficed in the former of these cases; it resulted in

permanent cure of a patient who had undergone, without successful results, 2 abdominal operations for the same symptoms ten and twelve years previously. In the other case, because of anomalies of the blood supply, nephrectomy was necessary, and performance of it resulted in cure. In 1 case of the series the diagnosis was made by means of intravenous urography and was confirmed by puncture and aspiration of the fluid contained in the cyst. In the other 5 cases, in which the patients were not operated on, the diagnosis was definitely made urographically and was substantiated by clinical observation. Gutierrez said it appears that when there are enough urologic symptoms and when the preoperative diagnosis has been made, the ideal course is to advise open surgical exploration of the kidney and the cyst by simple lumbotomy, with a view to resection of the cyst by a conservative operation. Then, in cases in which the kidney cannot be saved, nephrectomy will still remain as a last resort.

Tuberculosis.—McClelland and Davis [14] discussed the relationship between skeletal and genitourinary tuberculosis. They made a study of 297 cases of tuberculosis of bones and joints, which led to the discovery of 66 cases of tuberculosis in the genitourinary tract. In this group of 297 cases of tuberculosis of bones and joints, other tuberculous foci were present as follows: pulmonary tuberculosis, 41 per cent of cases; multiple skeletal tuberculosis, 29 per cent of cases; genitourinary tuberculosis, 22 per cent of cases; no other tuberculous lesion, 35 per cent of cases. Of the 66 patients, 44 were males and 22 were females. The resultant ratio almost coincides with the ratio of 3 males to 2 females which was calculated for the entire group of 297 patients. Among the 66 patients who had skeletal and genitourinary tuberculosis, 27 (41 per cent) were dead after an average period of observation of five years. The general death rate in the hospital for skeletal tuberculosis, complicated and uncomplicated, was 28 per cent during the same period. Therefore, they said, genitourinary tuberculosis is such a serious complication of tuberculosis of bones and joints that it increases the death rate by nearly 50 per cent.

McClelland and Davis said there is an 18 per cent chance that genitourinary tuberculosis will develop in patients who have a single skeletal tuberculous focus. Among the patients who have multiple skeletal lesions there is a 32 per cent chance that genitourinary tuberculosis will develop. Many patients suffering from genitourinary tuberculosis have had no symptoms.

Creevy [15] stated that renal tuberculosis may heal under proper hygienic management and reported a case of demonstrably bilateral, minimal, destructive tuberculosis. The patient was well eleven years after the apparent onset of the disease, and ten years after the last demonstrable bacteriologic evidence of activity of the disease. Calcium had been deposited in the zone of destruction on one side. Creevy expressed the opinion that healing may be said to have occurred only if pus and Mycobacterium tuberculosis have been recovered from a kidney which, at operation or necropsy after a considerable interval, contains a localized zone of destruction in which neither tuberculosis nor Myco. tuberculosis can be found. He did not believe that hygienic treatment is to be recommended as a substitute for nephrectomy except in an occasional case.

Surgical Technic.—Lazarus [16] described a maneuver designed to prevent injury to the diaphragm in cases of difficult nephrectomy. To reduce the period of con-

14. McClelland, J. C., and Davis, K. F.: The Relationship Between Skeletal and Genito-Urinary Tuberculosis, J. Urol. **47**:320-322 (March) 1942.

15. Creevy, C. D.: An Example of Apparent Healing of Bilateral Minimal Renal Tuberculosis, J. Urol. **47**:614-618 (May) 1942.

16. Lazarus, J. A.: A Simple Maneuver Designed to Prevent Injury to the Diaphragm in Cases of Difficult Nephrectomies, J. Urol. **47**:109-111 (Feb.) 1942.

valescence to a minimum and to avoid injury to the diaphragm to which the capsule might be adherent, the surgeon divided the capsule surrounding the upper pole of the kidney, leaving it attached to the under surface of the diaphragm and removed the rest of the capsule along with the kidney, to which it is intimately adherent. The kidney is exposed by means of the usual Albarran incision, which should be of a length which is ample for good exposure and which will facilitate necessary manipulation. A pad is placed in the lower angle of the wound, and by means of a deep retractor placed over it firm traction is exerted downward toward the symphysis. By this maneuver the kidney is drawn downward into the wound. After Gerota's capsule has been incised, the kidney is exposed in its fatty capsule and freed as far as possible from its bed, care being exercised to make certain that the upper pole, which is intimately adherent to the diaphragm, is not disturbed. A transverse incision is made on the anterior surface of the kidney as close to the upper pole as visibility will permit. This incision is carried down through the entire thickness of the capsule to the renal cortex. The upper and lower edges of the incised capsule are then grasped with clamps, and by means of a grooved director a line of cleavage is found between the inner surface of the true capsule and the renal cortex. Once this plane has been reached, Lazarus said, it is possible to introduce the right index finger into this space and with one sweep dislocate the upper pole of the kidney out of its capsule. The posterior reflexion of the capsule is then divided with a sharp scalpel, so that thereby the upper pole of the kidney is completely decapsulated. The procedure is completed by removal of the kidney with the rest of the capsule, which is attached to it.

Hypertension.—To determine how often hypertension and unilateral renal disease are associated, Baggenstoss and Barker [17] studied the records of 97 patients who came to necropsy. There were 84 instances of unilateral renal atrophy and 13 instances of unilateral hypoplasia. There were 48 cases of pyelonephritic atrophy, 28 of hydronephrotic atrophy, and 8 of pyonephrotic atrophy. The size of the heart and the condition of the opposite kidney also were studied in each case. Only in the cases of pyelonephritic atrophy (39.6 per cent) and of pyonephrotic atrophy (37.5 per cent) was the incidence of hypertension greater than in the authors' control group (29 per cent). The highest incidence of hypertension (41.9 per cent) was noted in cases of pyelonephritic atrophy in which the kidney weighed 75 Gm. or less. Evidence of inflammation in the opposite kidney was present more often in cases in which hypertension was observed. The degree of arteriosclerosis in the opposite nonatrophic kidney was generally less severe than that in the atrophied kidney. Baggenstoss and Barker expressed the opinion that these results suggest that unilateral pyelonephritic atrophy is more often associated with hypertension than would be expected on the basis of chance, and that hypertension is more likely to be present if the atrophy is severe. They suggested furthere that in many cases in which hypertension is in an early or mild stage it may not be associated with renal arteriosclerosis.

Friedman, Moschkowitz and Marrus [18] studied data concerning 193 patients who underwent nephrectomy for unilateral renal disease. The mean blood pressure and the incidence of hypertension were no greater in this group than they were in comparable control series of patients. No correlation was noted between the type of renal disease present and the presence of hypertension. After removal of the diseased kidney the blood pressure of the majority of patients remained essentially unchanged, whether the patients had been hypertensive or normotensive before

17. Baggenstoss, A. H., and Barker, N. W.: Unilateral Renal Atrophy Associated with Hypertension, Arch. Path. **32**:966-982 (Dec.) 1941.

18. Friedman, B.; Moschkowitz, L., and Marrus, J.: Unilateral Renal Disease and Renal Vascular Changes in Relation to Hypertension in Man, J. Urol. **48**:5-15 (July) 1942.

operation. In 22 per cent of the patients who had had normal blood pressure before operation, hypertension developed postoperatively. A significnat decline in blood pressure occurred in only 7 per cent of the patients who had had hypertension before nephrectomy. The incidence of hypertension was higher among patients who had good excretory function than it was among comparable patients whose excretion of urine from the diseased kidney was either poor or absent. Arteriolar sclerosis was found in the diseased kidneys of 82 per cent of the patients who had hypertension at the time of operation and of only 33 per cent of the patients who had a normal blood pressure at the time of operation but in whom hypertension developed after nephrectomy. The authors said that when unilateral renal disease and hypertension coexist, removal of the diseased kidney is not likely in the majority of cases to result in reduction of the blood pressure. The advisability of performance of nephrectomy in most cases should therefore be determined primarily by the nature of the renal disease rather than by the expectation that the blood pressure will be lowered thereby.

Shure [19] studied the incidence of hypertension among patients who had had pyelonephritis, his data consisting of those obtained in the performance of necropsy 11,898 times in a ten year period. Hypertension was found in 44.4 per cent of the cases, as compared with an incidence of 34.9 per cent in a control group of patients taken at random. After analysis, however, this greater incidence apparently related to patients who had bilateral pyelonephritis, and especially to men. It was most marked in relation to men more than 40 years old. The relative absence of high blood pressure among patients who had unilateral pyelonephritis was striking. The incidence of hypertension increased as the age of the patient increased, and was parallel to the incidence of advanced renal vascular damage. In small groups of patients who had polycystic kidney, horseshoe kidney and uncomplicated nephrolithiasis the incidence of hypertension was 46.15, 64.7 and 53.25 per cent, respectively.

In a review of renal disease as a factor in hypertension, Braasch [20] stated that of 4,000 patients who had hypertension, only 100 exhibited clinical evidence of a non-nephritic renal lesion. Only 19 of these patients, or less than 0.5 per cent of the total number of hypertensive patients, were selected for operation. He said that extensive investigation undertaken to rule out the kidneys as a cause of hypertension is not indicated unless there is definite clinical evidence of involvement of the urinary tract. Braasch found that chronic and atrophic forms of unilateral pyelonephritis, renal neoplasm, renal lithiasis, hydronephrosis, tuberculosis and polycystic kidneys, in the order given, are factors or causative factors in hypertension. The presence of renal stone or hydronephrosis, unilateral or bilateral, will not affect blood pressure unless there is secondary pathologic change in renal tissues. Best results from surgical treatment are obtained among young patients and when the hypertension is of comparatively recent origin. A permanent decrease in blood pressure was observed in only a third of the patients selected for operation. Braasch said there is no typical renal pathologic change observed in the presence of hypertension. The essential factor, in his opinion, is apparently an intrarenal vascular imbalance which permits the secretion of pressor substances.

Hyman and Schlossman [21] discussed the etiologic role of the intrarenal pelvis in hypertension. They found at necropsy of 55 patients who had had hypertension

19. Shure, N. M.: Pyelonephritis and Hypertension: A Study of Their Relation in 11,898 Necropsies, Arch. Int. Med. **70**:284-292 (Aug.) 1942.

20. Braasch, W. F.: Genitourinary Surgery: Renal Disease as a Factor in Hypertension, Am. J. Surg. **56**:209-215 (April) 1942.

21. Hyman, A., and Schlossman, N. C.: The Etiologic Role of the Intrarenal Pelvis in Hypertension, J. Urol. **48**:1-4 (July) 1942.

that the incidence of intrarenal and that of extrarenal pelves were similar. Review of 200 unselected intravenous pyelograms did not show that the incidence of hypertension among patients who had intrarenal pelves was higher than it was among those who had extrarenal pelves. In 71 patients who had renal calculi and hydronephrosis there was no relationship between the hypertension and the type of renal pelvis present. Hyman and Schlossman said that nephroptosis combined with an intrarenal pelvis does not appear to predispose to hypertension. They described experiments in which a quadrupedal animal with an intrarenal pelvis was placed in the upright position to simulate the relationships of the human kidney for a period of time sufficient for production of hypertension by other experimental means. The negative results of these experiments, as well as the results of studies of ureteral occlusion by other investigators, tend to show that the intrarenal pelvis does not play a causative role in clinical hypertension.

Renal Disease and Surgical Risk.—Odel [22] said that renal disease imposes an increased risk on the patient who comes to operation. In his general review of the subject, Odel pointed out the necessity for restoration of impaired renal function prior to surgical operation. Routine urinalysis and measurement of the volume of urine passed in twenty-four hours are valuable and simple preoperative tests. Determination of the concentration in the blood of urea, creatinine and chlorides, and determination of the carbon dioxide–combining power are valuable guides when renal impairment is more severe. Microscopic examination of the urine for erythrocytes, pus cells and organisms is indicated when renal infection is suspected. Mandelic acid and sulfonamide compounds are used in combating infection of the urinary tract. An increased oral or parenteral intake of fluid in the form of solutions of sodium chloride or of dextrose together with the use of theophylline with ethylenediamine promotes effective diuresis. Chlorides and sodium bicarbonate should be administered intravenously when they are indicated. The diet should be light and should contain a moderate amount of protein. Any patient who has renal disease and is to undergo an operation on the biliary or gastrointestinal tract should have the benefit of tests of hepatic function, Odel said. Spinal or local anesthesia is preferable from the renal standpoint. Postoperatively, measures must be taken to combat dehydration, oliguria, edema and anemia after the results of appropriate tests and determinations have established the causative factors of any of these conditions.

RENAL HYPERPARATHYROIDISM

Harrison [23] stated that urinary obstruction with imposed infection produces renal insufficiency, inducing hyperparathyroidism, with or without rickets, dwarfism or infantilism. Early recognition of the condition and relief from it achieved by the urologist are the only means thus far available to prevent this disease from progressing, Harrison said. It is of little benefit to the patient to remove obstruction, establish drainage and combat infection, when renal insufficiency has been established, with resultant changes. Harrison reported 5 cases, in 2 of which the patients died. Of the 3 patients who underwent operation and were living at the time of this report, 1 had a guarded prognosis with a solitary kidney and infection, and the other 2 were well and free of infection. One had attained a height of 6 feet (180 cm.) with no bony changes. The other had been growing at the rate of 2 inches (5 cm.) per year but was still stunted at the time of Harrison's report.

22. Odel, H. M.: Reducing the Surgical Risk in Patients with Renal Disease, Nebraska M. J. **26**:343-347 (Oct.) 1941.

23. Harrison, F. G.: Urinary Obstruction in Children Inducing Renal Hyperparathyroidism, J. Urol. **48**:44-57 (July) 1942.

RETROPERITONEAL TUMORS AFFECTING THE KIDNEYS

Sweetser [24] discussed retroperitoneal tumors influencing the kidneys and ureters and reported 8 cases of these neoplasms. He said that an accurate diagnosis is difficult to make. Before the days of intravenous urography it was impossible in most cases to rule out the possibility of renal tumor and to arrive at a definite diagnosis. Sweetser said that the patient's discovery of a mass usually not associated with abnormalities of the urine and not having the characteristic mobility of an intraperitoneal mass would lead to the physician's suspicion of retroperitoneal tumor or cyst. As a rule, an exploratory operation would be performed with the diagnosis still in doubt. In some cases the patient's history and the results of physical examination should strongly suggest the diagnosis. Sometimes the results of urinalysis, studies of the blood and roentgenograms may help. The perirenal insufflation of air and other gases has been advocated for the making of contrast roentgenologic studies, but Sweetser said that this procedure is of limited value because it is sometimes misleading and is not without dangers. He said that it should be used only as a diagnostic last resort, and observed that he would rather not use it at all. He expressed the opinion that at present urography, intravenous and retrograde, anteroposterior and lateral, provides the most valuable information of any diagnostic technic, but even with that help the difficulty of diagnosis is still recognized. In reviewing the possibilities of diagnosis, Sweetser stated that the patient's history may be of little or no value or it may give the vital bit of information. Physical examination sometimes discloses a mass that is definitely separate from the kidneys and does not move with respiration. Sometimes, associated findings, such as an enlarged spleen or large lymph nodes situated elsewhere than in the renal region, may be a guide. Usually, the results of physical examination do not clinch the diagnosis. The results of laboratory studies may help, but usually do not. Roentgenographic studies are of greatest value, especially when the urinary tract and the gastrointestinal tract are outlined and viewed from front and side. Sometimes, even in these days, the diagnosis may have to be made by exclusion and may have to await exploratory operation or necropsy. Sweetser said that since as a rule the only hope of cure of a primary retroperitoneal tumor is surgical removal, an operation is usually justifiable and indicated. It is true, however, that complete removal of the tumor may prove to be impossible because of extension and involvement of the great vessels or other essential parts.

In most cases, by far, the transperitoneal approach has been used, although the mortality rate accompanying this procedure has been much higher than that which accompanies an extraperitoneal approach. The justification for the transperitoneal approach has been the better visibility and accessibility claimed for it, but Sweetser said that the transperitoneal operation is associated with a definite risk of peritonitis and results often in extreme surgical shock arising from handling of the bowels and peritoneal surfaces, evaporation and other factors incident to such a prolonged and difficult operation. On the other hand, the lumbar and flank incisions, which seem to be considered by most surgeons as the only alternatives, have admittedly been unsatisfactory in that they have not provided adequate visibility or accessibility.

URETERS

Stone.—Kretschmer [25] reviewed a series of 500 cases of ureteral stone. He said that stone in the ureter is rare at the extremes of life. The youngest patient

24. Sweetser, T. H.: Retroperitoneal Tumors Influencing the Kidneys and Ureters, J. Urol. **47**:619-631 (May) 1942.

25. Kretschmer, H. L.: Stone in the Ureter: Clinical Data Based on Five Hundred Cases, Surg., Gynec. & Obst. **74**:1065-1077 (June) 1942.

in this series was 2 years old and the oldest 80. Stone occurred with the greatest frequency in the third, fourth, and fifth decades. Eighty-nine and four tenths per cent of the patients had a single stone, and only 53, or 10.6 per cent, had multiple stones. Stones in the ureter may vary in size, some being as small as a grain of wheat and others being of enormous size and weight. Hematuria may be the first and only symptom of which the patient complains. Furthermore, it should be remembered that stone is one of the five common causes of blood in the urine. In practically all the patients in this series, hematuria was followed by pain. Hematuria was present in 181 patients, or 34.2 per cent. The history of a previous passage of stones is most important. If a patient gives a history of having passed stones on one occasion or more, the odds are that he will pass stones again. Study of the roentgenologic findings in Kretschmer's series disclosed that positive reports for stone had been recorded concerning 455 patients, whereas the reports were negative concerning only 20 patients. Kretschmer said that the intravenous urogram is of much diagnostic aid. In the largest number of instances it reveals dilatation of the ureter and of the renal pelvis. Although dilatation (except when the stones are very small) is the rule, Kretschmer has seen a number of patients in whom the urograms disclosed no dilatation, despite the fact that the stones were far from being small. The urogram not infrequently reveals the ureter down to the bladder, or the outline may stop at the site of the stone, in this manner disclosing complete blockage.

A roentgenogram should be made of the renal region of each patient before operation; this procedure will avoid the embarrassment of the surgeon's operating only to find that the stone has progressed up the ureter or into the renal pelvis. Retrograde movement of the stone occurred in 10 patients in the present series. Kretschmer said that the treatment of stone in the ureter is naturally divided into three stages: (1) watchful waiting, (2) instrumental manipulation and (3) operative treatment. He said the fact should be borne in mind that many patients pass the stones without the use of instruments, by the simple expedient of drinking large quantities of fluids, with or without the taking of diuretic drugs. In Kretchmer's series 128 patients, or 28.9 per cent, passed stones without manipulation of any sort. He warned that manipulation of a stone with instruments is not entirely free from danger. In his series, 44.3 per cent of the patients passed the stone after manipulation. He said that during the past twenty-five years there has been a definite trend away from open operation in favor of cystoscopic manipulation. When a patient has a very large stone, it is perfectly obvious that manipulation is useless and that ureterolithotomy should be done at once. In case the patient has only two or three stones without complications, Kretschmer expressed the opinion that the urologist might wait or try manipulation before resorting to open operation. However, when complications are present, operation probably is the best procedure, although Kretschmer has seen patients with multiple stones pass them spontaneously. He said that a relatively large stone situated high in the ureter had best be operated for, whereas if a stone has descended into the pelvic portion of the ureter operation can be deferred while developments are awaited. If the onset of the symptoms is recent, the surgeon may wait, but if there have been recurrences without signs of remission, operation is clearly indicated.

In case severe reaction, such as pain, chills, fever and hematuria, occur after each instrumentation, the patient should be operated on. Operation is the only procedure to employ when severe attacks of hematuria, either with or without colic, occur and are accompanied by marked secondary anemia. On the other hand, when the patient has only an occasional loss of blood and mild secondary anemia, operation can be deferred to a later date. Kretschmer said that severe infection in

the kidney clearly indicates operation. Chronic pyelonephritis persists in the patients under consideration because of poor renal drainage, and should manipulation fail, operative removal of the stone is to be employed. Acute infection, unrelieved by drainage by ureteral catheter, necessitates operation at once. If the stone is large, this condition should be met with immediate removal; if the stone is small, drainage by ureteral catheter should be the procedure. In case drainage by catheter does not provide prompt relief, operation must be performed at once. Suppression of function above the anatomic situation of the stone does not call for immediate operation, since the opposite kidney will be able to maintain renal function. When complete hydronephrotic atrophy exists above the situation of the stone, operation should be performed. When moderately advanced hydronephrosis is present, the stone should be removed to prevent further progress of the hydronephrosis.

Cacciatore and Garcia [26] stated that there are many cases of ureteral lithiasis in which the results of routine roentgenologic examination of the urinary system are absolutely negative. They said that the frequency of occurrence of ureteral calculi that are invisible to roentgen rays is difficult to determine, since the literature on the subject is limited. In many papers the existence of such stones is mentioned and that is all. Cacciatore and Garcia protested against this manner of treatment of so important a subject, since the presence of a ureteral calculus is very different from the presence of a small caliceal or pelvic calculus. During the two years prior to the time of their report Cacciatore and Garcia systematically carried out intravenous urography on all patients who had renoureteral conditions. They regarded their results as of utmost importance in diagnosis. In 52 cases of ureteral lithiasis, 3 cases involved calculi which were invisible to the roentgen rays. This number represents 5.76 per cent, a figure the authors considered worthy of attention. In all 3 cases ureterolithotomy was carried out with excellent results. The means available for demonstration of these invisible stones are excretory urography, ureteral catheterization, retrograde pyelography and chromocystoscopy. Although these means of exploration may not permit visualization of the calculus, they will reveal the existence of "uroectasia" or retention of urine, the anatomic level at which the obstacle to evacuation is situated, its characteristics and the variations it undergoes from time to time. Cacciatore and Garcia said that if it is impossible to prove the existence of a ureteral calculus by direct visualization of the stone, an attempt should be made to demonstrate the dysfunction for which it is responsible. Among the types of dysfunction which may be present, uroectasia is the most frequent and the most important. Three illustrative cases were presented. They tend to show how misleading it is, on the basis of a plain roentgenogram of the urinary system, to consider the result "negative" when a calculus cannot be seen in the urinary system. On the other hand, the extraordinary value of excretory urography in cases of invisible calculus of the ureter is demonstrated, as is also the relative value of this form of exploration in cases in which the renal function, already seriously compromised, does not permit elimination of the opaque substance. The indispensability of ureteral catheterization and retrograde pyelography is also emphasized as a means of determining the precise localization of the ureteral obstruction and its character. Pneumopyelography is useless, since there is no air space around the calculus. All the observations gained from the aforementioned modes of exploration are important in cases of an obstructive renoureteral syndrome. Failure to make an exact diagnosis may lead to useless and even disastrous forms of therapy. Expectant therapy is especially condemned, because it may be responsible for irreparable damage to a kidney.

26. Cacciatore, C., and Garcia, A. E.: Los cálculos ureterales no visibles a los rayos X, Rev. argent. de urol. **10**:681-707 (Nov.-Dec.) 1941.

Muschat [27] discussed suprapubic ureterolithotomy. He uses a midline incision, which he has found gives satisfactory exposure with more safety and which consumes much less time than operations carried out by the old method of approach. In 1 case he removed two stones, one from each ureter, through the same incision. To do this by the old method he said, would have required two separate operations. A midline suprapubic incision is made which extends from the pubis to the umbilicus. The fascia is cut, and the rectus muscles are exposed and split, freed and retracted. The bladder is picked up with forceps and retracted to the opposite side. By blunt dissection, the upper corner of the bladder is free from the surrounding structures. The ureter is located in the upper end of the wound and can be picked up just as it leaves the covering of the peritoneum and becomes a free pelvic structure. This procedure is followed down to the ureteral vesical junction. A simple incision in the ureter is then made, and the stone is removed. The postoperative course usually is smooth, and there is very little abdominal or gastric reaction, probably because the peritoneum remains practically untouched.

Ureterointestinal Anastomosis.—Riba [28] reported a case of ureterointestinal anastomosis with an unusual complication. The patient was a girl 8 years old, who had exstrophy of the bladder. The ureter from the one good kidney (the right one) was transplanted to the colon. The left kidney was small and pyonephrotic and was removed. Two years after the second stage ureteral transplantation, the patient became uremic and very sick. The value for nonprotein nitrogen was elevated. Nephrostomy (right side) was performed, and a catheter was placed in the lower calix. The patient recovered from this operation readily. Later, a proctoscopic examination revealed that the site of the ureteral transplantation had become invaginated into the bowel. With an electric meatotome, this invagination or "rectal polyp" was incised, and this permitted the urine to pass freely through the anastomosis. The nephrostomy tube was then removed, and excretory pyelograms disclosed good function in the right kidney.

Ureterocele.—Thompson and Greene [29] reported a clinical study of 37 cases of ureterocele. In most cases this condition is of congenital origin, and it occurs much more frequently among women than among men. The ages of the patients varied from 9 to 64 years; the majority were between 30 and 50 years. The most common symptoms were pain, frequency of urination, dysuria, hematuria and passage of calculi. The diagnosis can always be determined by cystoscopic examination and only in an occasional case by excretory urography. The most satisfactory treatment, the authors said, is fulguration of the contracted ureteral orifice or a combination of ureteromeatotomy and fulguration of the wall of the ureterocele. Open operation is necessary in the presence of destroyed renal function or of urinary calculi which cannot be removed by transurethral methods.

Polyps.—Johnson and Smith [30] reported a case in which ureteral polyps had developed in a man 24 years old. The pyelograms disclosed hydronephrosis in the upper portion of the left ureter. There was a tear-shaped negative shadow on the basis of which the diagnosis of ureteral polyp was made. On surgical exploration the polyps could be felt just below the ureteral pelvic juncture. Nephrectomy was done, and the polyps were found to be similar to those occasionally seen in the nasopharynx.

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27. Muschat, M.: Suprapubic Ureterolithotomy, J. Urol. **47**:571-576 (May) 1942.
28. Riba, L. W.: Late Uretero-Intestinal Anastomosis Complication: Case Report, J. Urol. **47**:679-685 (May) 1942.
29. Thompson, G. J., and Greene, L. F.: Ureterocele: A Clinical Study and a Report of Thirty-Seven Cases, J. Urol. **47**:800-809 (June) 1942.
30. Johnson, C. M., and Smith, D. R.: Benign Polyps of the Ureter, J. Urol. **47**:448-452 (April) 1942.

Diverticulum.—Richardson [31] reported a case in which diverticulum of the ureter afflicted a woman 39 years old. The diverticulum originated from the middle third part of the ureter well below the renal pelvis and above the brim of the bony pelvis. There was no history of trauma to the ureter, infection of the urinary tract at any time, hematuria, passage of calculi or either renal or ureteral colic. At operation a no. 8 ureteral catheter was readily passed through the lower segment of the ureter into the bladder without meeting obstruction. Richardson said that repeated postoperative cystoscopic studies have demonstrated only that slight narrowing of the bladder segment of the ureter may be present, a narrowing which, however, permits the easy passage of ureteral catheters. It seems probable, therefore, that this diverticulum was of congenital origin. Its enormous size (3,500 cc. of urine by accurate measure was evacuated at operation) places it in a class by itself. Furthermore, Richardson said, his case is the only recorded instance of diverticulectomy in which double division of the ureter was required. It is also the only recorded instance in which after diverticulectomy an immediate and successful end to end anastomosis of the ureter was carried out, with subsequent restoration of function to normal. Richardson also reviewed the published clinical reports on this condition and summarized the data which they supply. He said that in the matter of priority, Lotsi was the first to report a diverticulum of the ureter in a living person; Neff shares with Hale and von Geldern the honor of having first diagnosed the condition with certainty prior to operation; and Teposu and Danicico were the first to demonstrate this lesion by means of excretion pyelography.

Of the recorded patients, 2 were less than 3 years old; 1 was 10 years old; 2 were in the second decade of life; 10 were in the third decade; 7 were in the fourth decade; 4 were in the fifth decade, and 2 were in the sixth decade. Richardson said that the sex was stated in 30 instances; in 15 cases the patients were male and in 15 they were female. The right side was involved in 13 cases, the left side in 14 and both sides in 1. In 17 cases the diverticulum was situated within 5 cm. of the site of the insertion of the ureter into the bladder; in 7 it was located from 5 to 10 cm. above the bladder; in 6 it had arisen adjacent to or within 4 cm. of the ureteropelvic junction. Preoperative diagnosis appears to have been made with reasonable accuracy in 28 cases by means of roentgenologic studies, cystoscopic investigations, including catheterization of the ureters, and retrograde pyeloureterography. In only 3 instances was a preoperative diagnosis arrived at by the use of excretion pyelography. Calculi were found in 8 of the diverticula. The formation of these calculi was promoted by infection and stagnation. Twenty patients had pain, colicky or dull, on the involved side; 19 had pyuria; 17 had frequency of micturition and dysuria; 6 had nausea and vomiting; 4 had hematuria; 4 had chills and fever. Richardson said there is, however, no characteristic syndrome. Treatment varied according to the requirements of and indications in the individual patient. For a few patients repeated dilation of ureteral strictures sufficed. Others required ureterotomy with dilation of the ureteral orifice. The majority, however, required a more radical procedure, such as diverticulectomy, diverticulectomy together with reimplantation of the ureter into the bladder, or nephroureterectomy. On the whole, the results have been satisfactory and creditable.

31. Richardson, E. H.: Diverticulum of the Ureter: A Collective Review with Report of an Unique Example, J. Urol. **47**:535-570 (May) 1942.

Spasm.—Lazarus and Marks [32] stated that ureteral spasm is a frequent finding in urologic practice. It may occur spontaneously or it may be associated with or initiated by a variety of conditions, among which ureteral calculus is the most frequent. It may occur in one ureter or both, either as a primary condition or as a secondary manifestation from some source of irritation which may be present on one side or both sides. Contralateral spasm presents an interesting and not infrequent condition occurring among patients who have unilateral renal or ureteral disease and may give rise to mild or severe symptoms. Relief of obstruction in one kidney usually results in spontaneous relaxation of the spasm in the opposite ureter.

BLADDER

Fistula.—Barnes and Hill [33] reported a series of 14 cases of intestinovesical fistula. The most common cause of this condition is diverticulitis of the large bowel, and the fistula and its underlying pathologic process frequently are not found, the patient being treated for what is thought to be "cystitis." Passage of gas from the bladder is almost diagnostic, and the cystoscopic appearance of a zone of edema and inflammation in the fundus of the bladder is the most characteristic observation. Cystograms, roentgenologic examination of the bowel and instillations of a dye may prove to be unsatisfactory as aids to diagnosis. Proctoscopic examination is preferable to roentgenologic study for the diagnosis of lesions in the terminal 10 inches (25 cm.) of the bowel. Surgical treatment is sometimes difficult, and the performance of preliminary colostomy is usually but not always preferable. Treatment should be administered for the prevention of postoperative peritonitis.

Counseller [34] called attention to the difficulty of closure of small vesicovaginal fistulas in certain situations, with particular regard to the vesical sphincter and ureters. Sulfanilamide and its derivatives have enhanced the treatment of vesicovaginal fistula in that the drug and its derivatives are able to destroy organisms in the urine in a much shorter period than had been possible formerly. It is thus possible to maintain the urine in a nearly sterile state during convalescence of the patient. This has been a very great asset in the improvement of end results. Meticulous care must be devoted to the patient during convalescence, to maintain the urine free from infection and to avoid incrustation in the bladder and occlusion of the catheter. The vagina should be cleaned of secretions daily. Ureterosigmoidostomy has a definite place in the treatment of huge vesicovaginal fistulas in cases in which the bladder has been rendered incapable of again retaining urine. Rectovaginal fistulas are best treated by complete excision of all scar tissue and reestablishment of the normal character of the rectum. Counseller expressed the opinion that particular attention should be directed toward those small fistulas which originate in an anal crypt, a circumstance in which it is essential that the surgeon understand the cause of the condition and the clinical course of the patient. Postoperative care is similar to that for patients who have undergone repair of vesicovaginal fistulas in that suture lines in both the rectum and vagina must be kept clean daily. This can be done by the use of a Sims speculum, a small anoscope and dry cotton swabs. Attention to these details will greatly increase the number of instances of primary healing.

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32. Lazarus, J. A., and Marks, M. S.: Ureteral Spasm with Special Reference to Contralateral Spasm of the Ureter: A Clinical Study, J. Urol. **48**:69-82 (July) 1942.

33. Barnes, R. W., and Hill, M. R.: Intestino-Vesical Fistula, California & West. Med. **56**:350-354 (June) 1942.

34. Counseller, V. S.: Surgical and Postoperative Treatment of Large Vesicovaginal and Rectovaginal Fistulas, Surg., Gynec. & Obst. **74**:738-745 (March) 1942.

Counseller [35] also discussed the various types of vesicovaginal fistulas in respect to some of the surgical problems involved in their repair. He said that the most important preoperative measure is cystoscopic examination of the bladder for determination of the amount of infection present, the direction of the fistula and its situation with respect to the trigone, urethral sphincter and ureteral meatuses. Postoperative care should include special measures, such as placing of the patient in the prone position on a Bradford frame above the surface of the bed, daily irrigation of the bladder and cleansing of the vagina. Culture of the urine should be done frequently in order to determine the bacterial count. Sulfathiazole and mandelic acid are extremely beneficial in the control of infection of the urinary tract.

Masson and Wilson [36] reported the results of their experience in the care of 48 patients who had a fistula between the urinary tract and vagina for which surgical repair was undertaken and 13 patients for whom operation was not performed. These patients were encountered from January 1937, to December 1939, inclusive. Thirty-three (69 per cent) of the 48 fistulas developed after surgical procedures and 13 (27 per cent) after childbirth. The surgical procedures included abdominal hysterectomy (23 cases), vaginal hysterectomy (3 cases), chemical hysterectomy (1 case), and other operative procedures (6 cases). In 1 case the condition had been caused by radium treatment, and in another, by congenital fistula. A vesicovaginal fistula was present in 40 cases, urethrovaginal fistula in 2 cases, ureterovaginal fistula in 2 cases and uterovesical fistula in 4 cases. That the condition may be difficult to cure is shown by the fact that 29 of the patients had undergone ninety operations, or more than three per patient, before they were seen at the Mayo Clinic. Only 19, or less than 40 per cent, had not undergone a previous operation. At the Mayo Clinic 38 (79.2 per cent) of the 48 patients underwent one operation and 7 (14.7 per cent) underwent two operations. Three patients underwent more than two operations. Masson and Wilson employed vaginal closure in 41 (85.5 per cent) of the cases. Abdominal closure was employed in 3 cases, transplantation of the ureter in 2 cases, and nephrectomy in 2 cases. Forty-two of the patients were cured by the operative procedures. One operative death occurred in this series. In the operative technic employed by Masson and Wilson emphasis is placed on the following points: (1) prone position of the patient, with the buttocks elevated during the operation; (2) adequate exposure, and (3) adequate mobilization of the vaginal flap and of the bladder, with closure with interrupted sutures without tension. The vesical and vaginal openings are closed separately in opposite directions. Postoperative insurance of continuous drainage of the bladder is accomplished by placing of the patient in the prone position on a Bradford frame.

Carcinoma.—Of 279 patients with tumor of the bladder treated with radon implants, Herger and Sauer [37] were able to trace 229 as to developments, clinical course and duration of radium reactions. Although late effects of radium therapy, such as telangiectases or stricture of the ureter, occurred infrequently, ulceration was observed in 195 (80.7 per cent) of the cases. In 53 instances such ulceration was complicated by the development of incrustations or stones or both. One

35. Counseller, V. S.: Some Urologic Phases of Vesicovaginal Fistula, J. Urol. **47**:711-720 (May) 1942.

36. Masson, J. C., and Wilson, R. B.: Fistulas Between Urinary Tract and Vagina, Minnesota Med. **24**:637-644 (Aug.) 1941.

37. Herger, C. C., and Sauer, H. R.: Occurrence and Clinical Course of Radium Reactions Following Use of Radon Implants in Treatment of Carcinoma of Bladder, J. Urol. **47**:141-147 (Feb.) 1942.

hundred and three of the ulcerations healed and 92 persisted either until death of the patient or until the time of the authors' report.

The statistical data presented indicate that the tendency toward the formation of ulcers is least with low grade malignant papillary carcinomas and greatest with papillary tumors of a high grade of malignancy, as well as with solid infiltrating cancers. Aside from the histologic aspects, the location of the lesion is important. Tumors which originate in the region of the vesical sphincter or center and border of the trigone have a substantial tendency toward the formation of persistent ulcers, whereas lesions of the anterior and posterior walls of the bladder are associated with a better prognosis as to development and healing of radium ulcerations.

For the determination of factors which influence the clinical course and duration of radium ulcerations, data on 179 patients who had single tumors were collected. The results of these studies show that the tendency toward persistence of radium ulcerations is in direct proportion to the size of the zone of implantation and to the amount of radium therapy delivered. The percentage of persistent ulcerations was 62.5 per cent for zones of from 4 to 5 cm. and 71.4 per cent for lesions larger than 5 cm. in diameter. If more than 300 millicurie hours of treatment was delivered to the tumor, persistence of the ulcer was observed in two thirds of the cases. The average duration of radium ulcerations among patients in whom healing of the ulcer took place was ten and six-tenths months. It was found that the duration of the ulceration was in direct proportion to the size of the zone of implantation and to the amount of interstitial radium therapy delivered. Radium ulcerations of the anterior and posterior walls of the bladder healed faster than those located in the fixed parts of the bladder. The development of incrustations or stones also prolonged the duration of the radium ulcers.

Barringer [38] reported that cancers of the bladder, both papillary and infiltrating, are well adapted for therapeutic attack by means of radon implants. Of 257 patients examined up to and including 1937, 112 had papillary cancers and 145 had infiltrating cancers. Excluding 15 patients, in most of whom metastasis had developed and palliative operation had been performed, 56.1 per cent of patients who had papillary cancer and 28.9 per cent with infiltrating cancers had been well for five years at the time of Barringer's report. When the two groups were combined, a five year rate of cure of 40.4 per cent was obtained. Both the suprapubic and the cystoscopic route have been used for the application of radon seeds, the latter route in about a fourth of all cases. The chief complications arising from the implantation of radon seeds are infection and formation of stones. These complications are becoming fewer as modifications are made in the original technic of implantation. Tumors of the vault of the bladder and extensive papillomatosis are better treated by means of operation alone. With all other types of cancer of the bladder radon implantation is more simple to effect, is associated with a lower operative mortality rate and provides more assurance of five year cure, Barringer said.

Fleischman and Mauritz [39] stated that adenocarcinoma of the urinary bladder is a rare pathologic entity. They said that Ash, in a careful analysis of 2,000 cases in the bladder tumor registry maintained by the Army Medical Museum for the American Urological Association, reported only 2 cases of this particular type of carcinoma. Two types of adenocarcinoma are recognized: (1) without colloid

38. Barringer, B. S.: Five Year Control of Bladder Cancers by Radon Implants, J. A. M. A. **120**:909-910 (Nov. 21) 1942.

39. Fleischman, A. G., and Mauritz, E. L.: Adenocarcinoma of the Urinary Bladder, J. Urol. **47**:658-663 (May) 1942.

degeneration and (2) with this type of degeneration, the latter being the type most frequently observed. The general characteristics of these tumors are not always the same. They vary in size, are usually sessile, appear frequently as flat, indurated lesions with ulcerated or necrotic zones and invariably infiltrate the deeper tissues. Histologically colloid adenocarcinomas are characterized by acini whose cell linings are of the high cylindric variety with basal nuclei which exhibit various stages of formation of mucin. Masses of mucin may be seen lying in the free spaces formed by the fibrous tissue. Fleischman and Mauritz said that the clinical observations made on a patient suffering from adenocarcinoma of the bladder differ in no way from those associated with neoplasms that are frequently found in the bladder, hematuria being the cardinal symptom. The usual dysuria and urgency and frequency of micturition invariably are present also. However, the clinical history may differ from that of other vesical neoplasms if the tumor has not penetrated the mucosa. An abdominal mass may be felt in the area of the bladder if the tumor is of unusual size. The authors said that such a tumor has been reported by Barringer. A tumor situated in the region of the trigone or vesical neck can be treated transurethrally. One situated at the apex of the bladder unquestionably cannot be removed satisfactorily by this method. It must be removed by suprapubic radical excision. Fleischman and Mauritz reported a case in which adenocarcinoma of the urinary bladder occurred in a white man 36 years old. The tumor was removed by means of the electrosurgical cautery. Extravesical extension was found later, and the patient died seven months after the operation.

Hemangioma.—Kahle, Maltry and Vickery [40] reported a case in which hemangioma of the bladder occurred in a woman 52 years old. At cystoscopic examination a papillomatous mass 1 cm. in diameter was seen in the region of the right ureteral orifice. A similar tumor was seen just above the trigone. The tumors were removed through a Stern-McCarthy resectoscope. The histologic report was "benign ulcerating angioma."

Glandular Proliferation.—Emmett and McDonald [41] stated that proliferative lesions of the urinary bladder which simulate tumor are occasionally encountered. Grossly, these lesions may closely resemble carcinoma, but histologic examination will show them to be composed of a proliferation of glandular tissue usually associated with inflammation. Emmett and McDonald, in the cases they studied, recognized two distinct types of glands: (1) the subtrigonal type (also called glands of Albarran), and (2) glands simulating those found in the intestine, which they called the "intestinal" type of glands. They said that the lesions seen in such cases have been described by many names, the most common of which is "cystitis glandularis." These glands are not apparent in the urinary bladder at birth and appear to be formed by metaplasia from the epithelium lining the urinary bladder. The presence of infection in all but 1 of the cases presented by the authors suggested that it is an important factor in the production of these glands.

Calculus.—Prentiss [42] presented a clinical analysis of two groups of similar patients who were suffering from vesical calculus treated by means of cystolithotomy or lithotripsy. He said the development of transurethral surgery has

40. Kahle, P. J.; Maltry, E., and Vickery, G.: Hemangioma of the Bladder: Report of an Additional Case, J. Urol. **47**:267-269 (March) 1942.

41. Emmett, J. L., and McDonald, J. R.: Proliferation of Glands of the Urinary Bladder Simulating Malignant Neoplasm, J. Urol. **48**:257-265 (Sept.) 1942.

42. Prentiss, R. J.: Vesical Calculus: Clinical Study Based on Two Hundred and Fifty Cystolithotripsies and One Hundred and Thirty-Two Cystolithotomies, J. Urol. **47**:664-671 (May) 1942.

eliminated most of the technical contraindications to lithotripsy and also all objections that the operation does not remove the associated obstructive causative factors of stone. The much reduced hospital stay and mortality rate, as well as the ease with which associated local conditions can be treated by means of the transurethral operation as compared with open attack on vesical calculus, justifies the readoption of the transurethral procedure as a proved, conservative method, Prentiss said.

Garcia [43] reported a case in which a man had a vesical calculus that had formed around a silk suture which had been placed in the wall of the bladder eight months previously, at the time of an operation, performed by another surgeon, for repair of inguinal hernia on the right. The patient described, with precise details, the placing of an indwelling urethral catheter at the close of the aforesaid operation, and the appearance of chills and fever in the days following, with pain in the hypogastrium and frequency of urgency to urinate, despite the presence of the catheter. Intense hematuria had been present for a week. At the end of two weeks, the signs of infection had disappeared, the pain had diminished and the urine was normal in appearance. The patient said he had been discharged after four weeks in the hospital, but micturition had not been normal since that time. Persistent pollakiuria with burning and tenesmus had been present since his discharge from the hospital. A plain roentgenogram of the bladder disclosed an oval shadow characteristic of a vesical calculus. When lithotripsy was attempted, it became apparent that the calculus was attached to the posterosuperior wall of the bladder, and this attachment made it difficult to grasp the stone. An attempt at traction produced hemorrhage, which prevented further endoscopic intervention. On the fourth day, the left epididymis became inflamed and a small abscess was found to require drainage. Two weeks later the calculus was removed from the bladder by cystotomy. It was found to be fixed to the right lateral wall of the bladder by a filiform pedicle. On extraction the stone was found to be 5 cm. in length; it closely resembled a snail, and was composed of three calculous masses, each distinct from the other and movable but all united by a flexible axis, along which they were strung. This axis, protruding at one end, was nothing other than the fragment of silk which had been placed, in a continuous suture, in the wall of the bladder to close a wound inflicted accidentally during herniorrhaphy eight months previously. That the suture was continuous could be shown clearly by the type of its uncovered terminus, the entire axis being more than 7 cm. in length. Garcia expressed the opinion that the case shows the untoward results that may follow the use of a nonabsorbable suture in a wound of the bladder and also the danger involved in the placing of a continuous suture in this structure. But whether a continuous suture is used or separate sutures are chosen, the outstanding lesson is that absorbable material should be employed. Otherwise, there is danger that the suture may serve as a foreign body around which, as a nucleus, mineral salts may collect.

Rupture.—Culp [44] discussed the treatment of ruptured bladder and urethra. He reviewed 86 cases of extravasation of urine, and made the therapeutic recommendations which follow.

Retrograde cystograms should be made in all cases in which rupture of the bladder is suspected and the correct diagnosis is not obvious. Physical observations

43. Garcia, A. E.: Cálculo vesical secundario a la sutura de la vejiga con material no reabsorbible, Rev. argent. de urol. **10**:709-716 (Nov.-Dec.) 1941.

44. Culp, O. S.: Treatment of Ruptured Bladder and Urethra: Analysis of Eighty-Six Cases of Urinary Extravasation, J. Urol. **48**:266-286 (Sept.) 1942.

alone may be disastrously misleading. Prompt operation, preferably carried out within two hours of the onset of extravasation, is imperative. Drainage by urethral catheter alone did not suffice to produce recovery for any patient who had the condition under consideration. Operation should consist of routine exploration of the peritoneal cavity, cystostomy and drainage of the perivesical tissues to as far as the base of the bladder. Culp said that the most common cause of death is peritonitis for which surgical exploration is not carried out. Retroperitoneal extravasation of urine was encountered frequently, but in such cases it was rarely possible to establish adequate drainage. The defect in the wall of the bladder should be repaired if possible, but this is not essential. The peritoneal cavity can be closed without the establishment of drainage after the evacuation of extravasated fluid, but drainage through stab wounds is the safer procedure. Rupture of the posterior urethra must be suspected in all cases of fracture of the pelvis. Complete division of the urethra at the prostatic apex is the most common type of injury. Cystourethrograms should be made in all cases in which the diagnosis is doubtful. Suprapubic drainage (established within four hours, if possible) should be routine. Retroperitoneal extravasation in which drainage was inadequate was the most common cause of death. Perineal anastomosis of the urethra or retrograde catheterization facilitates recovery. Culp said that urethral strictures must be dilated with care. In his series such instrumentation was responsible for most perforations of the anterior portion of the urethra. It is safer to use filiform bougies and followers than it is to use sounds. The contents of all periurethral abscesses should be drained, in view of the incidence of inflammatory perforation and subsequent extravasation of urine. Extensive drainage of regions in which extravasation has occurred and provision for adequate drainage of urine should be established within twenty-four hours of the onset of extravasation. Traumatic and inflammatory perforations present the same surgical problems. Perineal urethrotomy and suprapubic cystostomy (with or without retrograde catheterization of the urethra) are most valuable. Combined injury to the anterior and posterior portions of the urethra should be suspected in all cases of perforation near the triangular ligament. Suprapubic drainage should be instituted if any doubt arises as to pelvic involvement. Sulfonamide compounds should be administered orally and locally to all patients who can tolerate these drugs. Fluids should be administered intravenously in liberal quantities (judiciously) to combat or to prevent uremia and acidosis, which frequently complicate extravasation of urine.

CONGENITAL OBSTRUCTION OF THE NECK OF THE BLADDER

Thompson,[45] in discussing urinary obstruction of the vesical neck and posterior portion of the urethra of congenital origin, stated that the symptoms arising from congenital malformation of the vesical neck or posterior urethra seldom are apparent at birth. The onset of obstruction is insidious, and gross distention of the bladder does not appear early in the course of the disease. The urologist should suspect the presence of the condition while the amount of retained urine is still small. Renal insufficiency is a late manifestation. Recurring episodes of infection of the urinary tract should excite suspicion. Urographic evidence of obstruction will help to establish the diagnosis while renal function is still adequate. Thus, valuable glomeruli can be preserved. Thompson said:

> The deformity usually noted on cystoscopy is some condition other than valvular formations. The obstruction may be slight and the cystoscopist should look for the effects of obstruction,

45. Thompson, G. J.: Urinary Obstruction of the Vesical Neck and Posterior Urethra of Congenital Origin, J. Urol. **47**:591-601 (May) 1942.

such as trabeculation of the wall of the bladder, ureteropyelectasis and the like, rather than extreme deformity of the vesical neck or of the posterior urethra. Excision or destruction of what seems to be a minimal amount of tissue often will produce amazing results.

The postoperative treatment of infection is of paramount importance. The accumulation of residual urine cannot always be immediately abolished; great improvement in the tone of the detrusor muscle gradually will develop. It is best not to reoperate in any case until after edema incidental to operation has subsided. Catheterization during this period is sometimes necessary. Chemotherapy employed intermittently for a number of months postoperatively is best. Great improvement in the general health of the patient, restoration of normal urination and complete elimination of infection are possible when renal function has not been long impaired. Children affected by the condition are not always condemned to an early death, as has been alleged by some.

PROSTATE GLAND

Hypertrophy.—In another report Thompson [46] stated that transurethral prostatic resection is superior to other types of surgical treatment of the prostate gland. Recent developments in the resectoscope and better training of surgeons, he said, have eliminated objections to this method. In fact, so-called total prostatectomy can be more nearly accurately and effectively carried out through the urethra than by any other approach or means, with far fewer complications and a much lower mortality rate. Thompson reported on a series of 1,000 patients with various types of prostatic obstruction who were operated on by this method at the Mayo Clinic in 1939. In 40 cases two operations instead of one were necessary. Only 3.4 per cent of the 1,000 patients were less than 50 years of age, the average age being about 70 years. Heart disease was found in 22.8 per cent of the cases and hypertension in 28 per cent. Renal insufficiency was present in about a fourth of the cases. In 69.4 per cent of the cases the patient's postoperative temperature did not exceed 100 F. (37.7 C.). From the average patient who presented the ordinary type of prostatic enlargement the amount of tissue removed was 34.9 Gm. Thompson stated that the postoperative hospital stay is decidedly shorter than that required after other types of prostatic surgery have been carried out, and that complications occur infrequently. Of the 1,000 patients concerned, only 9 died; thus the mortality rate was less than 1 per cent.

Owens [47] compared the results of perineal prostatectomy and transurethral resection. He declared that the value of the transurethral method of prostatic surgery is now generally accepted. It has offered, he said, the first real challenge to the perineal approach for honors in the field of low mortality rates in surgical treatment of the prostate gland. The mortality record for perineal prostatectomy, when the operation has been properly done, has always been enviable; likewise, the late results of this operation have been excellent; but in the days when open operation was the only choice too many patients delayed their coming to the surgeon until their tissues were beyond recovery, even though the most skilful care might have been available. Owens said that thanks to transurethral resection the patient's fear of seeking relief has been removed, and, now that patients do come to the surgeon earlier than before, the type of care most suitable to their individual condition can be given them.

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46. Thompson, G. J.: Transurethral Prostatectomy, Urol. & Cutan. Rev. **45**:755-757 (Dec.) 1941.

47. Owens, C. A.: Perineal Prostatectomy and Transurethral Resection: A Comparison of Results, J. Urol. **47**:366-371 (March) 1942.

Thompson [48] discussed the subject of the patient with disease of the prostate who has marked renal insufficiency and in whom the content of urea in the blood is well over 100 mg. per hundred cubic centimeters. Such patients, he said, arrive with a greatly distended bladder but are still able to void. For this reason the bladder has not been drained previously, and in some instances the patient is unaware of the hugely distended bladder. Many times symptoms unrelated to the urinary tract cause them to seek medical attention. Often secondary anemia, weakness, drowsiness and vomiting are the presenting symptoms rather than difficulty arising from the urinary system. Thompson stated that in examination of such a patient the less trauma inflicted on the bladder and prostate gland the better, and said that he avoids making cystourethrograms or carrying out cystoscopy or retrograde pyelography. As a rule, a soft rubber catheter is used to drain the bladder; usually an inlying catheter or catheterization every six or eight hours constitutes a better method of treatment. The great majority of patients, however, can tolerate an inlying catheter, and such is the type of drainage employed until the output of urine is on the increase and there is great general physical improvement.

One patient with prostatic obstruction had a value for blood urea on admission of 410 mg. per hundred cubic centimeters. After two weeks of drainage by catheter, and with an output of urine of 3,500 to 4,000 cc. daily, the value for urea was still 160 mg. per hundred cubic centimeters. At this time transurethral prostatic resection was done, and 45 Gm. of tissue was removed in the usual manner. The patient's subsequent convalescence was smooth, and he left the hospital on the tenth postoperative day, at which time the value for blood urea had decreased to about 100 mg. per hundred cubic centimeters.

Thompson said he has not employed suprapubic cystostomy in these cases because in his opinion carefully managed drainage by urethral catheter can be carried on with less hazard to the patient than the aforementioned operation. In some cases secondary anemia is so advanced that it is necessary to transfuse blood before operation. He does not routinely employ any preoperative medication. If sulfonamide compounds are used they must be administered cautiously, for when renal function is greatly reduced the concentration of the drug in the blood usually increases rapidly. Thompson expressed the belief that the best type of anesthesia as a rule is low spinal anesthesia. However, in some instances in which the anemia has been extreme he has employed instead intravenous anesthesia produced with pentothal sodium. Drainage by catheter for five or six days postoperatively has been deemed wise. Because of the flaccidity of the bladder in these cases, it has been his rule to catheterize the patient six hours after the inlying catheter has been removed. In general, no matter how complete resection may be, retention of varying degrees is present for a number of days after removal of the catheter. For instance, a patient who had retained 5,400 cc. of urine had no desire to void for the first six or seven hours after the catheter had been removed. Finally, he voided a very satisfactory stream, but catheterization disclosed 600 cc. of retained urine. In the subsequent week the amount of retained urine gradually diminished to less than 60 cc. Shortly before publication of this report, Thompson received a letter from the patient's son (a physician), in which it was stated that the patient had no retention and that the urine was crystal clear.

The mortality rate in cases of this type is approximately the same as in cases in which an average condition is encountered. Thompson discussed the decrease

48. Thompson, G. J.: Prostatic Hypertrophy with Marked Renal Insufficiency, Urologists' Correspondence Club, Oct. 26, 1942.

in blood urea after transurethral removal of the prostate gland. In several patients the value for blood urea remained at from 80 to 90 mg. per hundred cubic centimeters even after six months' drainage by suprapubic cystostomy. However, when the prostate gland was enucleated, the value for urea immediately decreased to a value well below that which had obtained even with perfect drainage through the cystostomy tube. Probably the best explanation for this is that any type of artificial drainage is inferior to natural drainage.

Russ [49] presented 2 cases of prostatic obstruction in which the symptoms were predominantly gastrointestinal. He emphasized the fact that many lesions of the genitourinary tract may cause gastrointestinal symptoms which often lead to a delayed or an erroneous diagnosis. Thompson, in discussing these cases, stated that when the physician is confronted by an elderly man with bizarre symptoms he should always think of the possibility of urinary retention and resort to catheterization on the slightest indication.

PROSTATIC RESECTION FOR PATIENTS WITH TABES DORSALIS

Emmett and Beare [50] stated that bladder difficulties of tabetic patients are poorly understood. They reviewed the records of 419 patients who complained of such difficulties. Among males, aside from incontinence and the inability to determine when the bladder was full, the symptoms were similar to those caused by uncomplicated obstruction of the vesical neck. After studying the amount of residual urine in the bladder, Emmett and Beare concluded that in not more than 50 per cent of cases could the incontinence be attributed to overflow. Relaxation of the vesical neck was more common among the patients who had urinary incontinence, but with this single exception, the cystoscope disclosed nothing in their condition that was different from the condition of other patients in this group. Ten per cent of the males who had urinary difficulties underwent transurethral prostatic resection. Ten grams or less of tissue was removed in two thirds of the cases. The results of operation were very gratifying. No patients were made worse by the operation. Of 13 patients who had urinary incontinence prior to surgical operation, 11 were completely relieved of this condition. There are no clinical data which show that the external vesical sphincter itself is responsible for the difficulty. Emmett and Beare expressed the opinion that obstruction of the vesical neck, however slight, may produce disability among tabetic patients, whereas the same degree of obstruction may not cause any disability among patients who do not have tabes.

Carcinoma.—Belt [51] reported on 50 cases in which radical perineal prostatectomy had been done for early carcinoma of the prostate gland. In this group of 50 cases there were 2 postoperative deaths. In 19 of the 50 cases death occurred at a time remote from the time of operation and was caused by metastasis and by local recurrence of the neoplasm. In these 19 cases the extent of the disease was not recognized, because extension beyond the reach of surgical intervention must have occurred prior to the date of operation. Two of the 19 patients lived longer than five years; 2 more lived longer than four years; 2 lived longer than three years; and 4 lived longer than two years. Only 2 of these patients had stoppage of the urine before their death. In a second group, 19 patients were living at the time of Belt's report and exhibited no clinical or laboratory evidence of the existence of

49. Russ, F. H.: Urinary Obstruction and Gastro-Intestinal Symptoms: Report of Two Cases, Proc. Staff Meet., Mayo Clin. **17**:257-260 (April 29) 1942.

50. Emmett, J. L., and Beare, J. B.: Bladder Difficulties of Tabetic Patients, with Special Reference to Treatment by Transurethral Resection, J. A. M. A. **117**:1930-1934 (Dec. 6) 1941.

51. Belt, E.: Radical Perineal Prostatectomy for Early Carcinoma of the Prostate, J. Urol. **48**:287-297 (Sept.) 1942.

cancer. One of these patients had survived for more than fourteen years, another for more than thirteen years, another for longer than ten years, another longer than seven years and still another for longer than six years. Six patients had lived longer than five years; 1 had lived longer than four years and another longer than three years, at the time of Belt's report. Four patients were operated on more than two years prior to the time of Belt's report and 2 were operated on within two years before the time of the report. In the entire group of 50 patients, 10 had died in the years since operation from causes other than cancer of the prostate gland. When the procedure of radical perineal prostatectomy, as described by Belt, is employed, the patient is placed in the extreme lithotomy position. Antiseptic surgical preparation and draping include the fastening of a strip of rubber dam to the patient's skin with clips. This procedure excludes the anus from the surgical field. The curving line of incision is 1.5 cm. from the mucocutaneous juncture. The cut edge of the skin is pulled down, so that the fibers of the median raphe are stretched. These are cut, and the red, circular external rectal sphincter is easily pushed upward, away from the shining, white, longitudinal fibers of the rectum. The levator ani muscles are separated from one another in the midline. They are pushed laterally far enough to reveal the whole posterior aspect of the prostate gland. The vertical fibers of the rectum are depressed below the lower margin of the prostate gland. The lateral aspect of the prostate gland is separated from its bed by blunt dissection. The bundle of vessels which enter it at each lateral inferior border is isolated, ligated and cut between ligatures. A thin, tough veil of fascia which covers the seminal vesicles is incised transversely across the base of the prostate gland, so that the vesicles and ampullae which bulge beneath it are exposed. Seminal vesicles and ampullae are then bluntly dissected from their beds. The large blood vessel which enters each seminal vesicle at its apex is carefully ligated. A long strip of vas is dissected from the retrovesical tissues, to be removed with the specimen. Next, the apex of the prostate gland itself is approached. The gland is cut across, so that a collar of prostatic tissue remains attached to the membranous urethra, where circular muscular fibers encircle the canal. These fibers and the membranous urethra are carefully left undisturbed during the dissection. Dissection is carried forward between the anterior aspect of the prostatic capsule and in the rich plexus of veins which clings to it. The prostate gland now remains attached to the bladder by the mucosa at the neck of the bladder. This tube of mucosa is cut across with scissors, and the prostate gland, with capsule, both seminal vesicles, both ampullae and a long section of each vas, is lifted from the wound. The urethra and neck of the bladder are anastomosed. The urethral catheter is then inserted into the bladder. The tube of mucosa which forms the neck of the bladder and the tube of urethral mucosa formerly situated at the apex of the prostate gland approximate one another around this portion of the urethra. The thin fascial layer which covered the seminal vesicles and was incised transversely over them is now lifted up and stitched to the adventitia, which envelops the membranous urethra; next, the levator ani muscles are brought together with interrupted stitches. The edge of the rectal sphincter is brought into contact with the median raphe by means of a circular stitch. A slender tube of rubber dam is passed down to the posterior aspect of the bladder. The skin is closed with a running subcuticular stitch. The rubber drain is removed within twenty-four hours; the catheter, within seven days.

Ravich [52] discussed the relationship of circumcision to cancer of the prostate gland. He said that in a survey of prostatic operations performed by him from

52. Ravich, A.: The Relationship of Circumcision to Cancer of the Prostate, J. Urol. 48:298-299 (Sept.) 1942.

1930 to 1936 at the Jewish, Israel Zion and Beth El hospitals in Brooklyn, and from 1935 to the date of his report at the Adelphi Hospital, on patients whose ethnic status was readily available to him, the following data were obtained: (1) Of the total number of patients who had prostatic obstruction, 768 were Jews and 75 were non-Jews; (2) of the total number who had benign hypertrophy of the prostate gland, 755 were Jews and 60 were non-Jews; (3) of the total number of those who had a malignant process of the prostate gland, 13 were Jews and 15 were non-Jews. The incidence of cancer of the prostate gland among Jews was 1.7 per cent; among non-Jews it was 20 per cent. He expressed the opinion that such a striking difference in the same community is conclusive. Since morphologically Jews and non-Jews are alike, Ravich deduced that the circumcision of male Jews in infancy renders them relatively immune from cancer of the prostate gland in their old age. Cancer of the penis, which is said to occur exclusively among uncircumcised males, is apparently a lymph-borne disease originating from the irritating secretions that accumulate under the foreskin. In cancer of the prostate gland, however, this route may or may not be the one involved. Ravich stated his belief that it is entirely conceivable that the process may have as a basis some parasitic, viral or other carcinogenic agent that infests or involves the urethra and migrates along the lumen of this structure into the prostate gland in somewhat the same manner as that in which gonorrheal prostatitis so often complicates gonorrheal urethritis. Ravich said that another interesting observation had been made by the late Dr. John Osborne Polak, formerly professor of gynecology and obstetrics at the Long Island College of Medicine: that cancer of the cervix was found rarely among his Jewish patients, although it was rather common among non-Jews. This observation recently was substantiated by Frank R. Smith, in a study of cervical carcinoma made in the gynecologic service of a hospital. Such being the case, Ravich considered it conceivable that the disease is transmitted by direct contact to the wives of uncircumcised men during coitus.

Kahle, Ogden and Getzoff [53] reported 7 cases of adenocarcinoma of the prostate gland, in 6 of which the lesion was proved by biopsy. The patients had been treated during the two years prior to the time of this report with diethylstilbestrol or diethylstilbestrol dipropionate. To all the patients treated, this method of therapy brought prompt relief of pain and urinary symptoms and a general improvement in health. Two bedridden patients were restored to activity within four and six weeks, respectively, after the institution of treatment. Clinical improvement was associated in all instances with regression of the malignant lesion. At the time of the patients' last examination all the glands had lost their malignant characteristics, and the authors said it would have been impossible at that time to arrive at a diagnosis of carcinoma on the basis of rectal palpation. Clinical improvement was also associated with regression of metastatic lesions to the bones in the only case in which the making of serial roentgenologic observations was possible, and with regression of metastasis to the lymph nodes in the 2 patients who exhibited such lesions. Reduction in the size and alteration of the consistency of the primary neoplastic lesions, as well as reduction in the metastatic lesions, could be correlated readily with the marked retrogressive tissue changes observed in histologic study of specimens secured for biopsy after treatment.

53. Kahle, P. J.; Ogden, H. D., Jr., and Getzoff, P. L.: The Effect of Diethylstilbestrol and Diethylstilbestrol Dipropionate on Carcinoma of the Prostate Gland: I. Clinical Observations, J. Urol. **48**:83-98 (July) 1942.

Schenken, Burns and Kahle [54] reported on the results of histologic studies made in 6 cases of carcinoma of the prostate gland in which the patients were treated with diethylstilbestrol or diethylstilbestrol dipropionate. In 5 cases tissue was available for study before and after treatment. In 1 case tissue was not removed before treatment. In all 6 cases treatment was associated with definite regressive changes in the nucleus and cytoplasm of the tumor cells. The ultimate change which may occur in these neoplastic cells is undetermined.

TESTICLE, EPIDIDYMIS AND VAS

Tumors of the Testicle.—Twinem [55] reported on benign teratoma of the testicle in a boy 3 years old. His parents had noticed that enlargement of the right testicle had been present for two years before Twinem saw the patient. On examination, a painless, nontender, irregular tumor about 4 cm. in size was found in the boy's right scrotal sac. The testicle was removed through a right scrotal incision and found to be involved with a tumorous lesion which contained cartilage. Microscopic examination showed the lesion to be benign. Two years later the patient weighed 41 pounds (19 Kg.) and was in good general condition.

Rosenblatt, Grayzel and Lederer [56] discussed primary malignant tumors of the testicle. These tumors occur most commonly when the patient is between the ages of 20 and 50 years. The average incidence, according to age of the patient, of heterologous tumors shows that they develop earlier than do the homologous neoplasms. Bilateral tumors are rare, and the right side is usually more frequently involved than the left side. In Rosenblatt, Grayzel and Lederer's series, trauma apparently was a factor in 10 per cent of cases. The average duration of symptoms before medical advice was sought was fifteen months. Painless enlargement of the testicle was the most common symptom. The heterologous tumors are accompanied by a more unfavorable prognosis than are the homologous ones.

Wesselhoeft and Vose [57] discussed the surgical treatment of orchitis in mumps. They expressed the opinion that the early surgical treatment of orchitis in mumps accomplishes prompt relief from pain and saves the testicle from subsequent atrophy. In the follow-up examinations of 347 patients not operated on, atrophy was revealed in 190, or 54.7 per cent. Sterility as a result of atrophy is rare. Sterility is not to be confused with impotence, since sterility implies only a lack of sufficient sexual cells. Fear of sterility after the orchitis of mumps sometimes leads to a mental complex that may promote impotence. Twelve patients who had severe orchitis of mumps were operated on. The condition of 9 of these was followed for from six to twelve months after operation, and only 1 of the 9 patients was found to have any observable atrophy of the testicle. Wesselhoeft and Vose stated that the rationale of incision of the tunica albuginea in severe orchitis is somewhat comparable to that of paracentesis of a bulging, painful drumhead in otitis media. The operation must be done sufficiently early to avoid pressure necrosis in the testicle. It is useless to operate when the process is already on the wane. The operation is not indicated when orchitis is mild or when epididymitis predominates. An enlarged, hard,

54. Schenken, J. R.; Burns, E. L., and Kahle, P. J.: The Effect of Diethylstilbestrol and Diethylstilbestrol Dipropionate on Carcinoma of the Prostate Gland: II. Cytologic Changes Following Treatment, J. Urol. **48**:99-112 (July) 1942.

55. Twinem, F. P.: Benign Teratoma of the Testicle in a Three Year Old Boy: A Case Report, J. Urol. **47**:577-579 (May) 1942.

56. Rosenblatt, P.; Grayzel, D. M., and Lederer, M.: Primary Malignant Tumors of the Testicle, Am. J. Surg. **57**:94-103 (July) 1942.

57. Wesselhoeft, C., and Vose, S. N.: Surgical Treatment of Severe Orchitis in Mumps, New England J. Med. **227**:277-280 (Aug. 20) 1942.

tender testicle, associated with chills and fever, constitutes the indication for surgical intervention. Nitrous oxide and oxygen are the anesthetic agent of choice. An increase in temperature after operation signifies an invasion of some other organ by the virus.

Epididymitis.—Lich [58] prepared a local anesthetic agent in oil with nupercaine hydrochloride, which has anesthetizing properties of several days' duration. It induced an insignificant amount of cellular response when it was injected into the subcutaneous tissues of a dog. In a series of 147 cases this anesthetic agent in oil injected into the sheath of the vas promptly stopped the pain of acute epididymitis. The usual treatment for the primary cause of acute epididymitis is essential, since the injection therapy is but a symptomatic measure.

Tumors of the Spermatic Cord.—Prince [59] reported a case of angioendothelioma of the spermatic cord. Tumors occurring in the spermatic cord are rare. This case brings the total number of reported cases up to approximately 75. The patient was a man 63 years old who complained of swelling in the scrotum which he had first noticed about fourteen months previously. The testis on this side was found to be in the most dependent part of the sac and was normal except that from its upper pole there arose a firm, nodular, rounded mass 5 cm. in diameter. The testicle and tumor were removed. A diagnosis of "angioendothelioma of the spermatic cord with extension to the connective tissue of the cord at point of its division" was made.

PENIS

Anomaly.—Cochrane and Saunders [60] reported a case of duplication of the penis with an imperforate anus. Duplication of the penis or diphallus is a very rare anomaly. The baby was normal in every respect except for the genitalia and an imperforate anus. The penis was a well developed but unusual-looking organ with a double glans and a circumference of 3 inches (about 8 cm.) at the shaft. The right glans was the larger. Its length from the meatus to the corona was ⅝ inch (1.59 cm.); its circumference, 2 inches (2.5 cm.). The smaller glans was ⅜ inch (0.95 cm.) long and its circumference 1¼ inches (about 3 cm.). The scrotum was well developed, and the testes were normal and completely descended. The scrotal circumference was 5½ inches (about 14 cm.). There was a somewhat redundant prepuce on the left which partly covered the glans on that side. The prepuce on the right was poorly developed. A frenum was demonstrable on both the right and the left side of the glans. Exploration of the urethra was carried out with no. 5 F. ureteral lead catheters. The catheter introduced in the meatus of the left or smaller glans was inserted into the bladder without difficulty. Two drachms (7.5 cc.) of clear amber urine was obtained. The catheter in the right urethra was arrested after it had been passed for 1 inch (2.5 cm.). A roentgenogram made at this stage with the catheters in situ seemed to indicate that the right urethra was blind and that it had no connection with the bladder. It was later observed that while normal urination occurred through the left meatus 4 or 5 drops were passed from the right during the act of micturition. Later the bowel was opened. A month after operation the baby was progressing favorably.

58. Lich, R., Jr.: The Treatment of Acute Epididymitis with Nupercaine in Oil, J. Urol. **47**:196-198 (Feb.) 1942.

59. Prince, C. L.: Malignant Tumors of the Spermatic Cord: A Brief Review with Presentation of a Case of Angio-Endothelioma, J. Urol. **47**:793-799 (June) 1942.

60. Cochrane, W. J., and Saunders, R. L. de C. H.: A Rare Anomaly of the Penis Associated with Imperforate Anus, J. Urol. **47**:818-823 (June) 1942.

McCrea [61] reported a case of congenital absence of the penis. Congenital absence of the penis, like diphallus, is an exceedingly rare anomaly. Only approximately 10 authenticated cases have been previously reported. McCrea's patient was a youth 19 years old. Examination of the genitalia revealed that the penis was totally absent. The scrotum was normally placed. It presented a somewhat bifid contour. The testicles were of normal size; the right one was situated slightly lower than the left one. The distribution of the pubic hair was typically masculine. Results of examination of the perineum revealed nothing abnormal except a small elevation about 1 cm. in front of the anterior anal margin. This elevation was soft and pliable; through this eminence urination was accomplished. The patient had complete urinary control. Rectal examination revealed a prostate gland that was normal in contour and size. However, at the anal margin a distinct tubular structure could be palpated; this structure was considered to be the urethra, since it could be distinctly traced to the eminence on the perineum.

URINARY ANTISEPTIC AGENTS

Cook [62] reviewed recent advances in the chemotherapy of infections of the urinary tract. Mandelic acid is effective if the urine contains at least 0.5 per cent of the drug at a p_H of less than 5.5. Gram-negative bacilli and Streptococcus faecalis can be destroyed when these conditions are satisfied. Sulfanilamide, azosulfamide (disodium 4-sulfamidophenyl-2′azo-7′-acetylamino-1′-hydroxynaphthalene-3′,6′-disulfonate), sulfapyridine and sulfathiazole are effective against the usual gram-negative bacilli and beta hemolytic streptococci. Since sulfonamide compounds are more effective in alkaline mediums, they have been useful in combating organisms which split urea, notably bacilli of the Proteus type. Sulfapyridine is of some value in destroying staphylococci and micrococci, but sulfathiazole is the most effective compound in this group. When Str. faecalis is present, mandelic acid is the drug of choice. More than 90 per cent of patients who have uncomplicated infections of the urinary tract can be treated effectively with these drugs, provided there is no cicatricial deformity in the kidney, or other complication. Any stone, tumor, foreign body or obstructive formation must be removed before chemotherapy can be used effectively. Likewise, chronic prostatitis must be dealt with by other means if a coexisting infection of the urinary tract is to be relieved by chemotherapy. If the kidney is poorly functioning, azosulfamide can be administered with the least danger, and mandelic acid should not be given. Sulfonamide compounds usually are administered orally in four divided doses amounting to 40 to 60 grains (2.6 to 4 Gm.) daily for periods varying from eight to fourteen days. Close observation of patients receiving sulfonamide compounds is necessary for the detection of any toxic manifestations. If treatment is not effective after two or three courses of chemotherapy, complete urologic study is indicated.

Helmholz [63] found that sulfathiazole is bactericidal for Escherichia coli in concentrations lower than those which are bactericidal for any of the other organisms commonly found in the urinary tract, and that sulfathiazole acts therapeutically in doses ranging from 0.75 to 1.0 Gm. (about 12 to 15 grains) per day in an average instance. It is Helmholz' opinion that the administration of sulfa-

61. McCrea, L. E.: Congenital Absence of the Penis, J. Urol. **47**:818-823 (June) 1942.

62. Cook, E. N.: Recent Advances with Chemotherapy in the Treatment of Infections of the Urinary Tract, New England J. Med. **226**:187-190 (Jan. 29) 1942.

63. Helmholz, H. F., and Larson, N.: Concentration of Sulfathiazole at Which Bactericidal Action Is Lost for Bacteria Commonly Present in Urinary Infections, Proc. Staff Meet., Mayo Clin. **16**:404-408 (June 25) 1941.

thiazole in doses of 0.13 Gm. (2 grains) five times a day will prevent the bacterial infections commonly associated with postoperative catheterization. When this dosage is used and when the output of urine is 1,000 cc. per day, it is possible to provide a concentration of the drug in the urine of between 20 and 30 mg. per hundred cubic centimeters.

Helmholz [64] gave directions for the clinical administration of methenamine, mandelic acid, sulfanilamide and sulfathiazole as indicated by recent developments in chemotherapy in the treatment of infections of the urinary tract. In the presence of badly damaged kidneys, sulfathiazole in doses of as little as 1 grain (0.065 Gm.) a day has brought about striking effects in the appearance of the urine. Because of the inhibitory effect of small doses of sulfathiazole on nearly all types of organisms, with the notable exception of Str. faecalis, Helmholz suggested that this compound be used as a prophylactic agent against postoperative infections of the urinary tract. He pointed out that sulfathiazole may be effective against Str. faecalis at concentrations of less than 30 mg. per hundred cubic centimeters of urine, provided the p_H is 5.5 or less.

Strom and Thompson [65] administered sulfathiazole prophylactically to 100 consecutive patients who had undergone transurethral prostatic resection, and compared the clinical response of the patients to the response of a similar number of patients who did not receive sulfathiazole. Sulfathiazole administered prophylactically (7½ grains or 0.48 Gm.) four times daily was found to lessen the postoperative febrile reaction and the number of complications. The authors urge caution in the use of sulfathiazole among elderly patients because of the potential danger of toxic reactions.

Rottino and La Rotonda [66] reported a case in which death followed the administration of sulfadiazine for pneumonia. A total of 61 Gm. of sulfadiazine was administered during a period of eleven days, but a value for the drug in the blood of 20.7 and 23 mg. per hundred cubic centimeters was maintained. After this the patient complained of dysuria, and the urine contained erythrocytes and sulfadiazine crystals. On the first examination the urine had been clear. The patient died rather suddenly after two days of abdominal distention. Both kidneys were found to be large and congested, and the microscopic examination disclosed numerous crystals. Study of the kidneys disclosed changes in the excretory and secretory tubules and glomeruli. Most excretory tubules were dilated, some to such an extent that they had herniated and ruptured through the perirenal capsule covering the hilar surface of the kidney. Within their lumens was found a variety of substances: polymorphonuclear leukocytes, coagula and crystals. Polymorphonuclear leukocytes were found in large numbers in some tubules. Crystals were best demonstrated in sections prepared by frozen section. They appeared large and fan shaped. Glomeruli were numerous and large. Many were ischemic, although their capillaries appeared to be widely dilated. Epithelial and endothelial cells seemed well preserved, swollen but not hyperplastic. An occasional glomerular capillary was adherent to Bowman's capsule.

64. Helmholz, H. F.: Recent Developments in the Treatment of Urinary Infections, Southwestern Med. **25**:286-289 (Sept.) 1941.

65. Strom, G. W., and Thompson, G. J.: The Effect of Sulfathiazole on Febrile Reactions Following Transurethral Prostatic Resection, Proc. Staff Meet., Mayo Clin. **17**:241-256 (April 22) 1942.

66. Rottino, A., and La Rotonda, O.: A Fatal Human Case of Urolithiasis Medicamentosa Caused by Sulfadiazine, J. Urol. **48**:310-317 (Sept.) 1942.

Greene, Pool and Cook [67] treated 42 patients who had various types of infection of the urinary tract with sulfadiazine, in divided doses of 3 Gm. or less administered daily. Esch. coli and micrococci were the most common organisms, although others were encountered. In 24 cases (57 per cent) the urine was rendered sterile and in 12 cases (29 per cent) improvement was noted. Complete failures occurred in 6 cases (14 per cent). In a few cases, sulfadiazine was found to be as effective as sulfathiazole in the treatment of gonorrhea. In conclusion, they stated that sulfadiazine is slightly less effective and more expensive, but less toxic, than sulfathiazole.

Bandler and Bruger [68] discussed suppression of urination caused by sulfathiazole. The most common complications are hematuria, oliguria and anuria, renal insufficiency, and precipitation of crystals in the tubules, renal pelves, ureters and bladder. They reported a case in which suppression of urination and retention uremia were caused by sulfathiazole, with recovery of the patient achieved by ureteral manipulation, pelvic lavage and an increased intake of fluids.

UROGRAPHY

Findley, Edwards, Clinton and White [69] stated that intravenous urography can be converted into a satisfactory test of renal function by determination of the quantity of iodine which appears in the urine under standard conditions. Normal persons excrete approximately 45 per cent of the injected dose of 3,5-*diiodo*-4-pyridone-*N*-acetic acid and diethanolamine (diodrast) or a compound of this contrast medium in thirty minutes, and reductions in the rates of excretion of iodine are roughly proportional to variations in the clearance of urea.

ANESTHESIA

Nesbit [70] stated that the ideal anesthetic agent for urologic instrumentation should fulfil several requirements. It should relieve apprehension, which causes the patient to exaggerate all painful stimuli. It should also effectively prevent painful stimuli from reaching the higher centers and should blot out the memory of pain. It should be a short-acting agent to facilitate full postcystoscopic cooperation of the patient and should not produce nausea or other unpleasant sequelae which might be as objectionable as the averted pain. Furthermore, the ideal anesthetic agent should have a wide margin of safety and be inexpensive and easily administered. A new field for clinical investigation has been opened by the advent of intravenous anesthetic agents. Anesthesia produced with pentothal sodium has been used for three years and fulfils most of the requirements that have been enumerated. In an effort to utilize the distinct advantages of anesthesia with pentothal sodium and to eliminate the disadvantages of that agent, Nesbit devised a technic of administration of it for urologic instrumentation which has proved so satisfactory as to approach the requirements that have been set up for the ideal anesthetic agent. The actual technic of administration is as follows: Preoperative medication, consisting of the hypodermic injection of ⅙ grain (0.01 Gm.) of morphine sulfate, is administered to the patient on call. The patient is prepared for cystoscopic examination in the usual manner and a small bore needle is

67. Greene, L. F.; Pool, T. L., and Cook, E. N.: Sulfadiaziine in the Treatment of Infections of the Urinary Tract, Proc. Staff Meet., Mayo Clin. **17**:497-512 (Sept. 23) 1942.

68. Bandler, C. G., and Bruger, M.: Urinary Suppression Due to Sulfathiazole, New York State J. Med. **42**:1627-1630 (Sept. 1) 1942.

69. Findley, T.; Edwards, J. C.; Clinton, E., and White, H. L.: Intravenous Urography: A Test of Renal Function, J. Urol. **48**:119-125 (July) 1942.

70. Nesbit, R. M.: Pentothal Analgesia, J. Urol. **47**:738-740 (May) 1942.

introduced into the vein in the arm. Administration of a 2.5 per cent solution of pentothal sodium is then begun; the solution is administered slowly. Usually, the patient states that he is sleepy after from 6 to 10 cc. of the anesthetic agent has been administered. When the patient says he is very sleepy, the examining physician replies: "I am now going to pass an instrument which you will feel. It will not hurt you. You are to remain quiet and relaxed while I am carrying out this examination." So saying, the examining physician passes the instrument and conducts the examination. The anesthetist continues to administer small amounts of the anesthetic agent as required during the examination in order to keep the patient entirely cooperative. At the end of the examination, when instruments have been removed, administration of the anesthetic agent is stopped and within a few seconds' time the patient is conscious and entirely willing and able to cooperate with any instruction which is given.

TUBERCULOUS BACILLURIA

Ordway and Medlar [71] discussed tuberculous bacilluria. They accumulated data over a ten year period on the presence of Mycobacterium tuberculosis in the urine of clinically tuberculous and nontuberculous patients. Results of a total of 1,074 inoculations of guinea pigs, with sediments from twenty-four hour specimens of urine obtained from 287 tuberculous patients and 112 nontuberculous patients, have been recorded. Of the tuberculous patients, 22 (7.7 per cent) had urine which contained Myco. tuberculosis. Of these, 17 (77 per cent) had no clinical symptoms suggestive of renal tuberculosis. Leukocytes and erythrocytes in urinary sediment do not necessarily indicate the presence of Myco. tuberculosis. The presence of this organism in the urine does not indicate that progressive renal tuberculosis will inevitably follow. Surgical intervention should therefore be delayed until such a time as progressive renal destruction has been proved.

Myco. tuberculosis is not commonly found in the urine, even in cases of far advanced pulmonary tuberculosis, and can be demonstrated repeatedly in some cases in which tuberculous infection has not been suspected.

HEMATURIA

Cahill [72] presented a review of the various diagnoses arrived at in a urologic service and the occurrence of hematuria as a symptom among the conditions diagnosed. Cahill's figures show that hematuria is a serious symptom, and that in the majority of cases it is associated with some serious lesion, such as tumor, infection or calculus. A study of 89 cases in which the cause of hematuria was not apparent after a first investigation indicated that sooner or later reinvestigation showed a cause for the hematuria to be present in 55 of these cases. There is also a group of cases of so-called essential hematuria in which various pathologic lesions will be found or no pathologic lesions at all will be found.

URINARY CONCRETION

Posey [73] described certain lesions of the renal papillae resembling the calcium infarct. These lesions were found in 66 instances in 340 consecutive necropsies, exclusive of infants less than 3 weeks of age, stillborn babies and subjects on whom only partial necropsy had been carried out. In 39, or 59 per cent, of the cases

71. Ordway, W. H., and Medlar, E. M.: Tuberculous Bacilluria: A Ten Year Study, J. A. M. A. **119**:937-942 (July 18) 1942.

72. Cahill, G. F.: Hematuria: Its Clinical Significance, J. Urol. **47**:224-234 (March) 1942.

73. Posey, L. C.: Urinary Concretions: II. A Study of the Primary Calculous Lesions, J. Urol. **48**:300-309 (Sept.) 1942.

in which papillary lesions were present there were grossly recognizable stones and in only 6 of these cases had the patient ever had symptoms of calculous disease. The papillary lesion was observed in renal pyramids when phosphate, oxalate or urate stones were present. The papillary lesions probably precede actual clinical calculous disease, and other factors, such as stasis, infection and avitaminosis, may contribute to the development of calculi so formed. The condition appears to be primary vascular degeneration, which is probably different from ordinary atherosclerosis, since it may be present in the absence of recognizable atherosclerosis. It is suggested that the vascular degeneration seen in the primary calculous lesion of the renal papilla may be related to hyperexcretion of an insoluble urinary salt.

Balch [74] stated that the development of urinary calculi during pregnancy is rare, only 3 instances of such calculi being found in 36,101 deliveries. Three cases are reported; in 2 the calculi were renal and in 1 they were ureteral. The most likely reason for such a low incidence is pelvic and ureteral dilatation, which allows free passage of any formations of crystals. Ureteral atony which occurs during pregnancy no doubt is the reason for the fact that ureteral colic is so rare. Renal and ureteral operations seldom cause miscarriages, nor do they cause a greater mortality rate among gravid women than they do among nongravid women. Pregnancy at any stage does not increase the technical difficulties of removal of stones in the kidney or upper half of the ureter, but it is practically impossible to carry out surgical treatment of the lower part of the ureter during the last trimester. Cystoscopic manipulation of ureteral calculi during pregnancy is not recommended, except in selected cases.

Tests for Concentration of Urine.—Kottke, Code and Wood [75] undertook to determine the power of the kidney to do its work in general and its ability to excrete excess chloride in the absence of the adrenal cortical hormone, but with the animal in good condition and maintained on a diet high in sodium and low in potassium. Dilution of the urine and tests of concentration and a test of renal chloride concentration were carried out on dogs before and after adrenalectomy. Results of their experiments indicate that the ability of the kidney of the adrenalectomized dog to dilute urine, that is, to reabsorb the crystalloids and leave the water of the glomerular filtrate, is not impaired by the operation. On the other hand, results of tests of concentration indicate that the power of adrenalectomized dogs, maintained on a diet high in sodium and low in potassium without cortical hormone, to concentrate urine, that is, to reabsorb water selectively, is reduced even when these animals are in excellent general condition.

In the performance of tests of the concentration of chloride, it was found that there is a tendency for the rate of production of urine in the adrenalectomized animals to increase slowly to a maximum and to remain fixed at this level throughout the test. This fixed rate of production of urine, as a rule, was less than the maximal rate of production of urine observed in intact animals. The maximal concentration of chloride was limited in the adrenalectomized animals to less than 11.6 Gm. per liter of urine, whereas in the intact animals the concentration increased to considerably higher values. Likewise, the maximal output of chloride per minute was always less in the adrenalectomized animals than in intact animals. These results would indicate some reduction in the power of the tubular function of the kidney which is amply supplied with sodium chloride but which is deprived of cortical hormone to concentrate chloride in the urine.

74. Balch, J. F.: Urinary Calculus Associated with Pregnancy: A Consideration of Management with Report of Three Cases, J. Urol. **47**:705-710 (May) 1942.

75. Kottke, F. J.; Code, C. F., and Wood, E. H.: Urine Dilution and Concentration Tests in Adrenalectomized Dogs, Am. J. Physiol. **136**:229-243 (April) 1942.

The Production of Diuresis.—To determine the effect on the renal tubules of the repeated intravenous injection of an 8 per cent solution of sucrose in half-strength Ringer's solution as a measure to produce diuresis, Helmholz and Bollman [76] used 7 rabbits and 4 dogs in their experiments. In both species the most striking changes in the urine or urinary system, as well as in the values for phenolsulfonphthalein and urea, were noted after the first injection. These changes were temporary, and repeated injections produced neither the same acute changes nor any permanent damage in the histologic structure or the function of the kidney. Although the tubular epithelium seemed to be considerably changed histologically after the injection of this solution, it seemed able to function. The appearance of casts, albumin and sometimes erythrocytes in the urine was likewise temporary. Rabbits can excrete from 90 to 100 per cent of fluid when it is given in the form of an 8 per cent solution of sucrose in half-strength Ringer's solution at a rate of 100 cc. per kilogram of body weight per hour for a six hour period. Such injections can be repeated as often as every other day. Dogs can excrete 80 per cent of the fluid when it is given at a rate of 50 cc. per kilogram of body weight per hour for a six hour period weekly. In neither animal do the kidneys exhibit any permanent damage after multiple injections of the solution, and they regain their normal histologic structure within ten days. Helmholz and Bollman concluded that this solution can be used justifiably in clinical emergency conditions in which the rapid production of diuresis is desired.

ENDOCRINE THERAPY

Kearns [77] stated that pellet implantation offers a desirable and safe means for the administration of testosterone to patients who are dependent on testosterone replacement therapy or who are greatly inconvenienced by visits to the physician's office, because of either their remote location or their hours of work. Apparently there are no objections to this form of treatment. In a considerable number of cases (approximately 85 in which such implantation has been carried out during the past two years) no untoward effect has been observed, and it was Kearns's belief that it is a safe procedure.

HERMAPHRODITISM

Chanis [78] discussed some aspects of hermaphroditism and reported a case of female pseudohermaphroditism. The patient was a Negro 18 years old. At birth, the attending physician had declared the patient to be a male. From the age of 12 years onward the patient had had occasional penile erections. At 14 years of age small amounts of blood had been passed in the urine monthly. At 16 years the patient apparently was sexually a normal male. Urination and evacuation of semen had been accomplished through an orifice in the scrotum. Physical examination disclosed a normal penis except that the urinary meatus ended blindly in a pouch 3 cm. long. There was a small opening in the base of the scrotal raphe, through which the urine was voided. Testicles could not be palpated. The mammary glands were well developed. Surgical exploration of the abdomen disclosed a small uterus with two tubes, and two well developed ovaries were seen. Testicles were not found. Subtotal hysterectomy was done, and later a plastic operation on the breasts was carried out. A follow-up report secured a year later indicated that the condition of the patient apparently was more satisfactory than before.

76. Helmholz, H. F., and Bollman, J. L.: Intravenous Use of Sucrose-Ringer's Solution to Produce Maximal Diuresis, J. Lab. & Clin. Med. **27**:606-615 (Feb.) 1942.

77. Kearns, W. M.: Pellet Implantation of Hormones in Urology, J. Urol. **47**:587-590 (May) 1942.

78. Chanis, D., Jr.: Some Aspects of Hermaphroditism: Report of a Case of Female Pseudohermaphroditism, J. Urol. **47**:508-514 (April) 1942.

News and Comment

American Urological Association.—A meeting of the American Urological Association will not be held this year, in view of the fact that the government is discouraging the holding of all conventions except those primarily of military interest. The $500 research prize which is offered annually by the association will therefore not be awarded this year.

Meeting of International College of Surgeons.—The Fourth International Assembly of the International College of Surgeons will be held June 14 to 16 at the Waldorf Astoria Hotel, New York. Dr. Fred H. Albee, of New York, is the international president, and Dr. Max Thorek, of Chicago, the international executive secretary. Dr. Manuel A. Manzanilla, of Mexico, and Prof. Herman de las Casas, dean of the University of Caracas, Venezuela, will serve as chairmen of the program coordination for Central and South America, and Dr. Rudolph Nissen, of New York, will act for Europe. The rehabilitation committee is composed of Drs. Fred H. Albee (New York), William D. Ryan (Detroit) and Custus Lee Hall (Washington, D. C.). Dr. A. A. Berg (New York) is chairman of the program committee; Dr. Charles Phillips (New York), chairman of the arrangements committee; Dr. Chester A. Peake (Brooklyn), chairman of the exhibit committee, and Dr. Milton Bodenheimer (New York), chairman of the publicity committee.

Examination by American Orthoptic Council.—The next examination by the American Orthoptic Council will be held in September and October 1943.

The written examinations will be held at various cities in the country on September 9. Only those passing the written examinations will be permitted to take the oral and practical tests, which will be given in Chicago on October 9.

Applications on official forms should be addressed to the American Orthoptic Council, 23 East Seventy-Ninth Street, New York, for receipt before Aug. 1, 1943.

Reprints of "Progress in Orthopedic Surgery" Available.—Arrangements have been made whereby reprints of "Progress in Orthopedic Surgery for 1941," which appeared in the September, October, November and December 1942 and January 1943 issues of the ARCHIVES OF SURGERY, may be procured at $1 a copy. Checks should be made payable to Dr. A. R. Shands Jr. and sent to 535 North Dearborn Street, Chicago.

CORRECTION

In the article by Drs. Davis, Frank, Hurwitz and Seligman entitled "Intravenous Use of Vitamin K_1 Oxide," in the February issue (ARCH. SURG. **46**:296, 1943), figures 2 and 3 (not the legends) are reversed.